STUDY TO VALIDATE THE ACCURACY OF HEARTS3 SCORE IN RISK STRATIFYING CHEST PAIN IN THE EMERGENCY ROOM

A Dissertation Submitted to

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For the Award of the Degree of

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GOVERNMENT KILPAUK MEDICAL COLLEGE

CHENNAI

MAY 2019

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This is to certify that **"STUDY TO VALIDATE THE ACCURACY OF HEARTS3 SCORE IN RISK STRATIFYING CHEST PAIN IN THE EMERGENCY ROOM"** is a bonafide work done by **Dr. R. NARAYANEE** Post graduate student, Department of General Medicine, Kilpauk Medical College, Chennai-10, under my guidance and supervision in partial fulfilment of rules and regulations of the Tamil Nadu Dr. M.G.R Medical University, for the award of M.D. Degree Branch I (General Medicine) during the academic period from MAY 2016 To MAY 2019

Prof. Dr. K.V. RAJALAKSHMI M.D.
Professor and Head of the Department,
Department of Medicine,
Govt.Kilpauk Medical College ,
Chennai – 10.

Prof. Dr.T.S.SANTHI,M.D.
Guide for the study,
Professor & unit Chief
Department of Medicine,
Kilpauk Medical College

PROF. P. VASANTHAMANI,
MD., DGO., MNAMS., DCPSY., MBA
DEAN
Government Kilpauk Medical College & Hospital
Chennai – 600 010

DECLARATION

I solemnly declare that this dissertation **"STUDY TO VALIDATE THE ACCURACY OF HEARTS3 SCORE IN RISK STRATIFYING CHEST PAIN IN THE EMERGENCY ROOM"** was prepared by me at Government Kilpauk Medical College and Hospital, Chennai, under the guidance and supervision of **Prof. Dr. T. S.SANTHI, M.D,** Professor of General Medicine, Department of Internal Medicine, Government Kilpauk Medical College and Hospital, Chennai. This dissertation is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai** in partial fulfilment of the University regulations for the award of the degree of **M.D. Branch I (General Medicine)**.

Place: Chennai-10 **Dr. R. NARAYANEE**

Date :

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Prof. Dr. S.CHANDRASEKAR., M.D.
Guide for the Study,
Professor and Unit Chief,
Department of Medicine,
Govt. Kilpauk Medical College,
Chennai.

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The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval *" TO VALIDATE THE ACCURACY OF HEARTS3 SCORE IN RISK STRATIFYING CHEST PAIN IN THE EMERGENCY ROOM"* submitted by Dr.R.Narayanee, Post Graduate in General Medicine Govt. Kilpauk Medical College, Chennai-10.

The Proposal is **APPROVED.**

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

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Chennai-10.

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TABLE OF CONTENTS

INTRODUCTION

Chest pain is a very common presentation at the Emergency room.

The causes could range from benign, non life threatening ones to those that jeopardize life. Acute Coronary Syndrome is one common cause of chest pain belonging to the latter. Only 15-25% of patients with chest pain actually have ACS[17].

Many a time, there is a doubtful situation in categorising patients with non ST elevation chest pain with regards to whether to follow them up or to evaluate them aggressively or discharge them. While it is too expensive to evaluate every such patient, discharging prematurely a patient with an impending Acute Coronary Syndrome is a serious professional misconduct.

Though there are many scores like TIMI, GRACE which helped in prognosticating an established acute coronary event, there was not an objective method available to risk stratify patients presenting with chest pain, to aid further decision namely early discharge or observation or intervention.

Then, in 2008, in Netherlands, Six et al put forward an objective method to risk stratify patients quickly, using minimum resources, called the HEART Score, utilising the History, ECG finding, Age, Risk factors, Troponin – all taken down on the spot at presentation. This score has been well validated by prospective studies.

But the HEART score had some shortcomings such that the components were not given weightage in the score as per their importance. Hence to improve on the HEART score, the Erlanger HEARTS3 Score[1], which uses likelihood ratio analysis to give appropriate weight to the individual elements of the HEART score as well as incorporating 3 additional variables viz, Sex, Serial 2^{ND} hour ECG, and Serial 2^{ND} hour Troponin during the initial emergency room evaluation was made.

AIM

The aim of my study is to risk stratify Non ST elevation chest pain patients in the Emergency Room using HEARTS3 Score, so that high risk patients can be evaluated and low risk patients can be discharged early, so that the resources need not be spent in evaluating all patients.

OBJECTIVES

The objective of my study is to

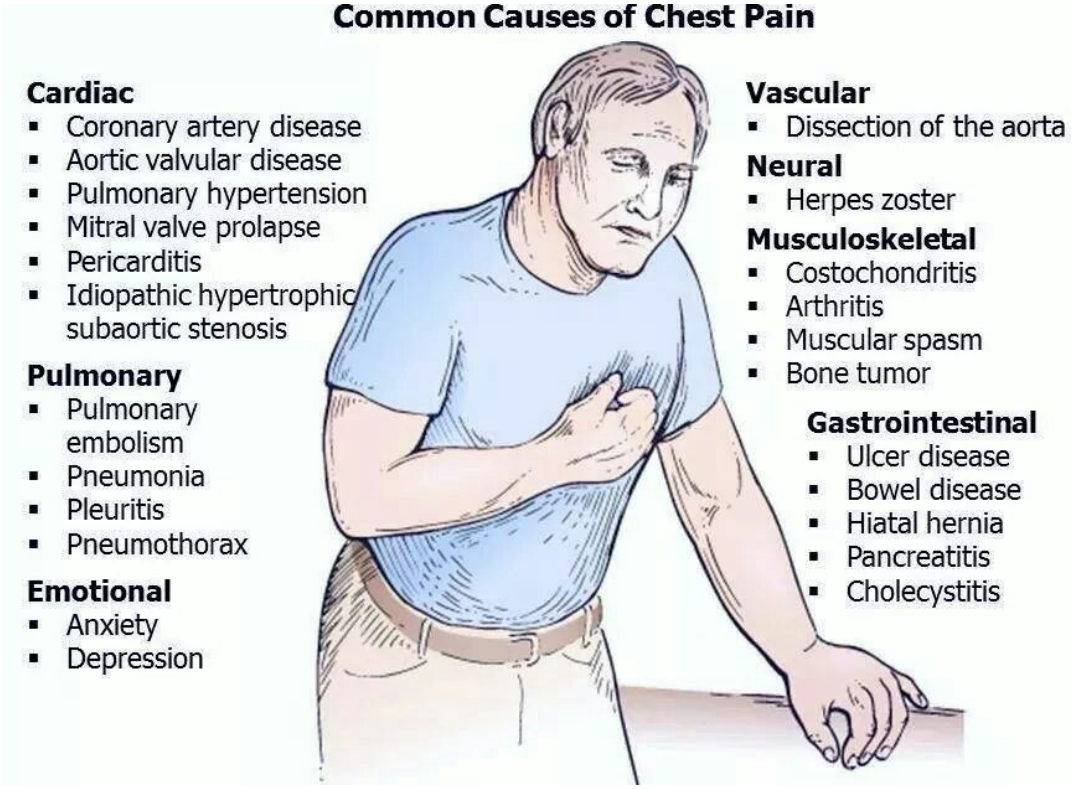
- Determine the association between the HEARTS3 score and outcome in the form of Major Adverse Cardiac Event such as Myocardial Infarction, Cardiogenic shock, Cardiac arrest, all cause cardiac death upto 7 days in all patients presenting with non ST Elevation chest pain to the Emergency Room and
- Validate the accuracy of the HEARTS3 Score in risk stratifying such patients.

REVIEW OF LITERATURE

CHEST PAIN

According to CDC report of 2005[2], Chest pain accounts for about six million annual visits to Emergency Departments in the United States, making chest pain the second most common complaint.

The potential sources of chest pain could range anywhere from the skin upto the endocardium, including esophagus, stomach, abdominal viscera.



Of the above mentioned causes, the life threatening causes which require immediate and prompt timely identification include:

- Coronary Artery Disease as Acute Coronary Syndrome
- Pulmonary embolism
- Pneumothorax
- Dissection of aorta
- Pancreatitis
- Hollow viscus rupture including esophageal tear.

The Myocardial ischemic pain due to Acute Coronary Syndrome is the commonest of the above mentioned dangerous etiologies of chest pain.

Pain originating from deeper visceral structures are poorly localised by the Central Nervous System due to common representations on the somatosensory cortex.

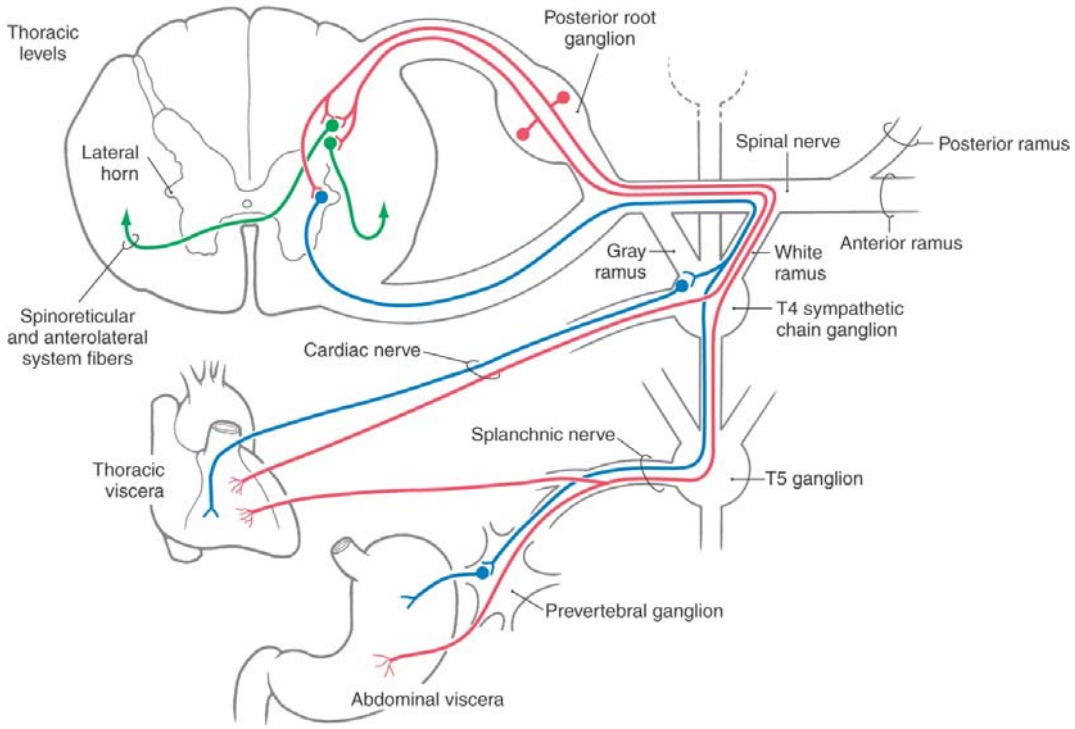
NEUROLOGY OF CHEST PAIN.[7,8]

The pain originating from the viscera of the thorax namely the heart , lung (visceral pleura), oesophagus, great vessels are taken by the autonomic nerves.

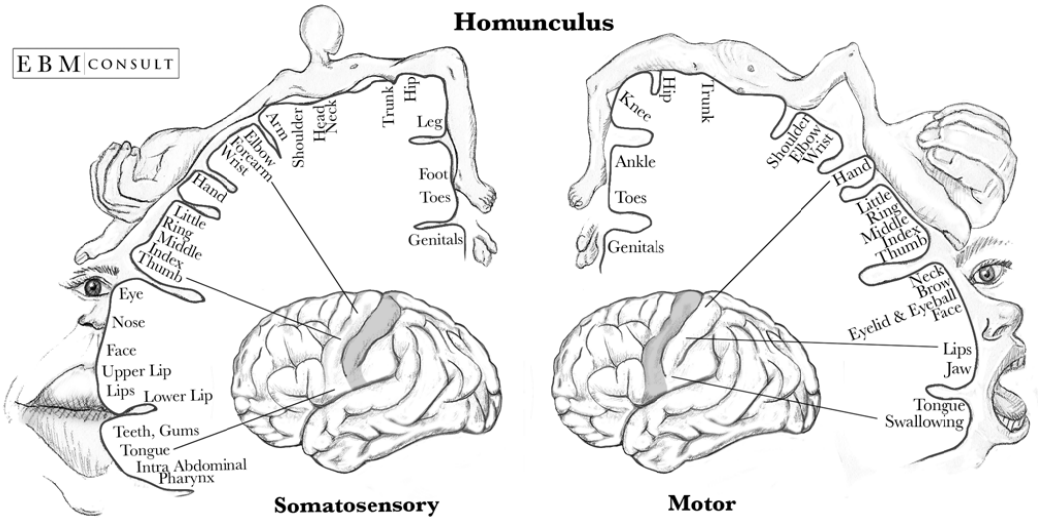
With respect to the pain of myocardial origin, the pain is taken by sympathetic nerves that pass via the superior and inferior cardiac plexus, via cardiac nerves, pass through the sympathetic ganglia without synapsing to enter

into the spinal nerve via the white rami communicantes, enter the dorsal root ganglia of T1 to T4 spinal segments.

After Entering the spinal cord, the fibres ascend some two segments above and enter the posterior grey horn to terminate in the 2nd order neuron in Rexed lamina I and V. From there, the second order neurons cross over to the contralateral side and ascend in anterior spinothalamic tract.



The pain of visceral origin is poorly localised because, the viscera are poorly represented in the sensory homunculus in the post central gyrus.



Another reason is the concept of convergence. The number of spinothalamic tract fibres are lesser when compared to the number of nociceptive afferent fibres. Hence many visceral and somatic nociceptive fibres synapse on a common dorsal grey horn cell to form the spinothalamic tract.

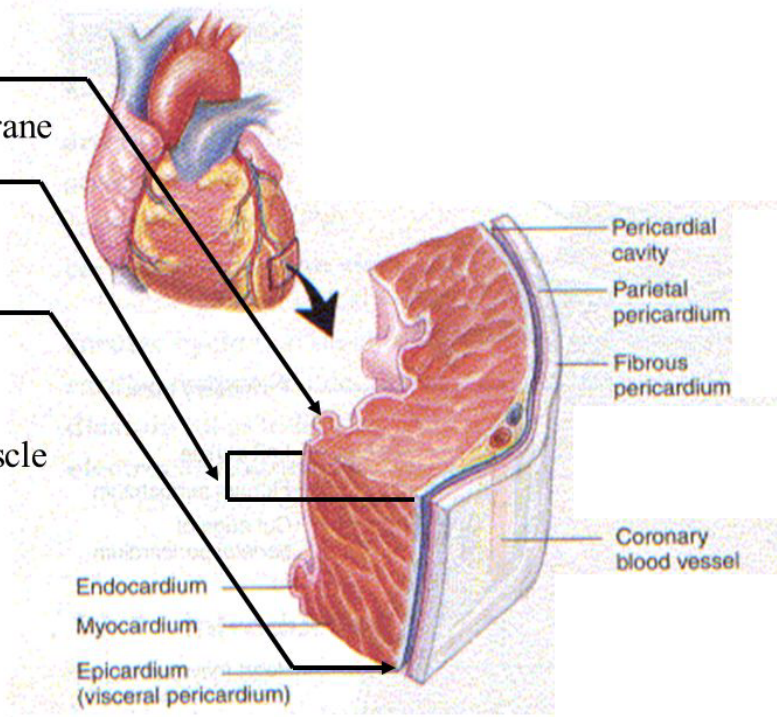
The myocardium especially has a paucity of sensory nerve endings. All these factors are responsible for poor localisation of visceral pain in general and cardiac pain especially.

MYOCARDIAL BLOOD SUPPLY

The blood supply to the myocardium at rest is about 0.8 ml/gram/ minute. The epicardial coronary arteries send penetrating end arterial branches to the myocardium that penetrate the thickness of the myocardium to reach the innermost aspect of it. The endocardium gets its blood supply from the blood within the chamber.

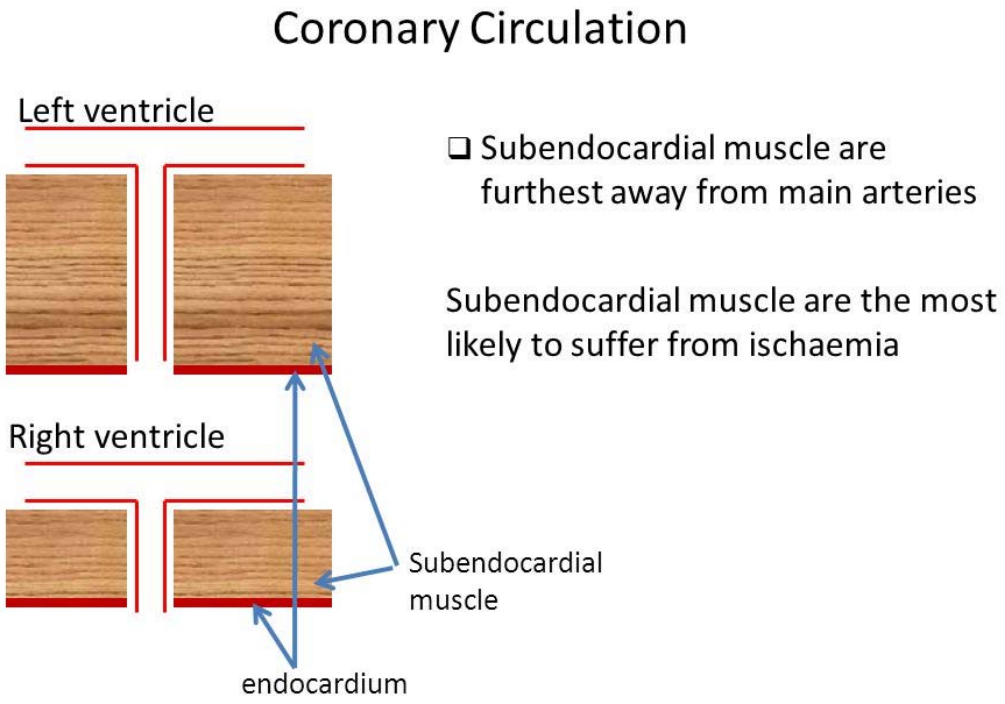
D. Wall of the Heart

1. endocardium
   a. serous membrane
2. myocardium
   a. thick cardiac muscle layer
3. epicardium
   a. epithelial and connective tissue
   b. specialized muscle fibers - Purkinje fibers

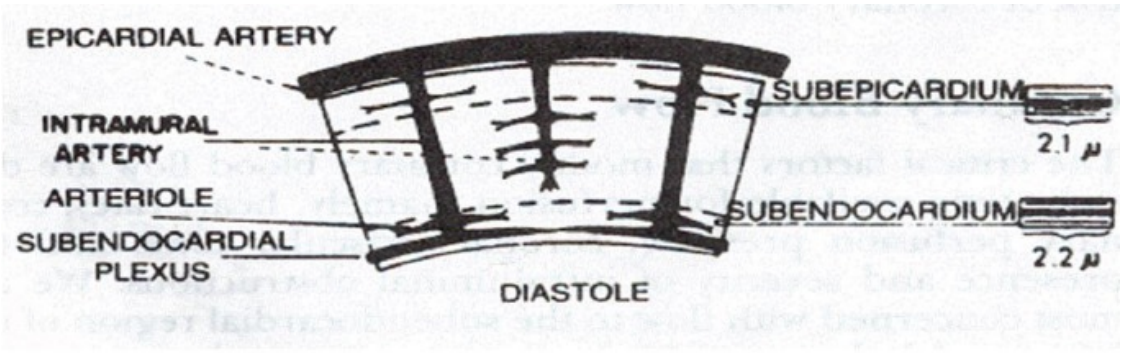


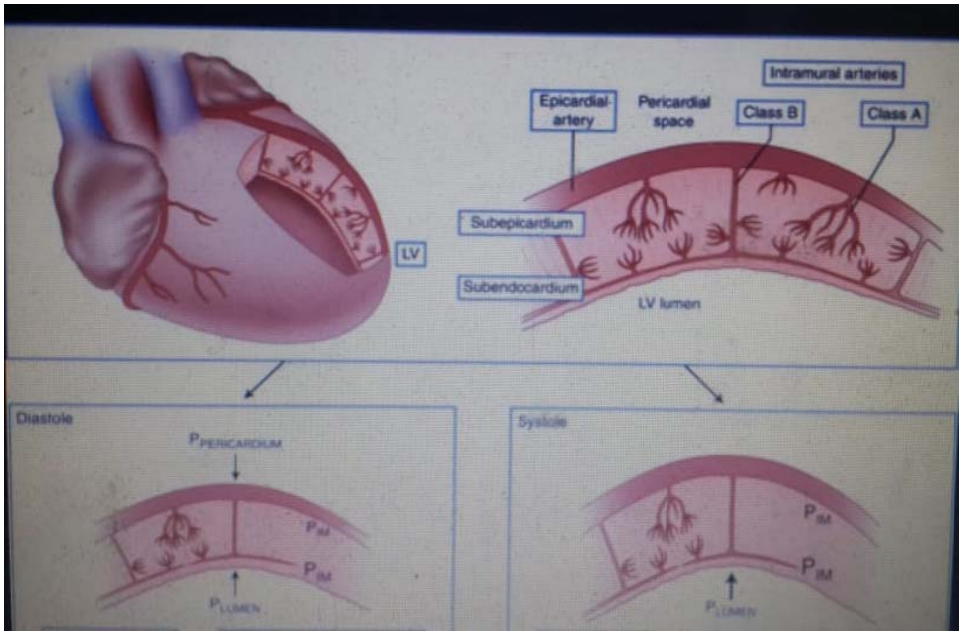
All organs receive their blood supply during systole. But the myocardium is perfused during diastole because, as the penetrating branches from the epicardial coronaries traverse the thickness of the myocardium, they get occluded by the myocardial contractive sheer during the systole.

The left ventricle owing to its greater myocardial muscle mass, the left ventricular blood vessels traverse a longer distance through the myocardium than those of the right ventricle. This is depicted in the following diagram.

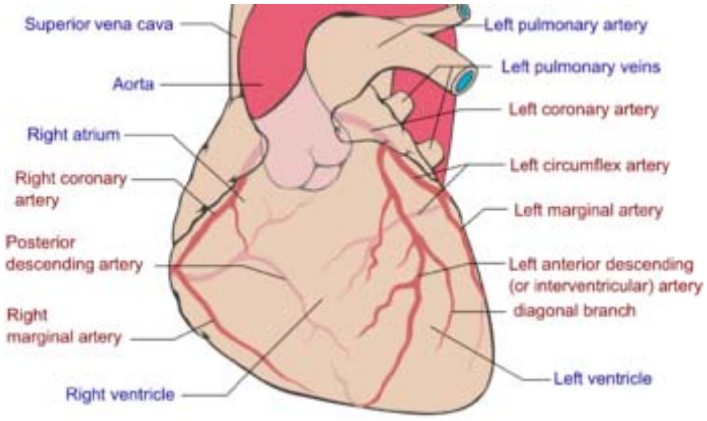


Owing to the pattern of blood vessel arrangement, the subendocardial region is the most ischemia prone region. Though being end arteries, the penetrating branch ramifies to form a subendocardial arterial plexus.

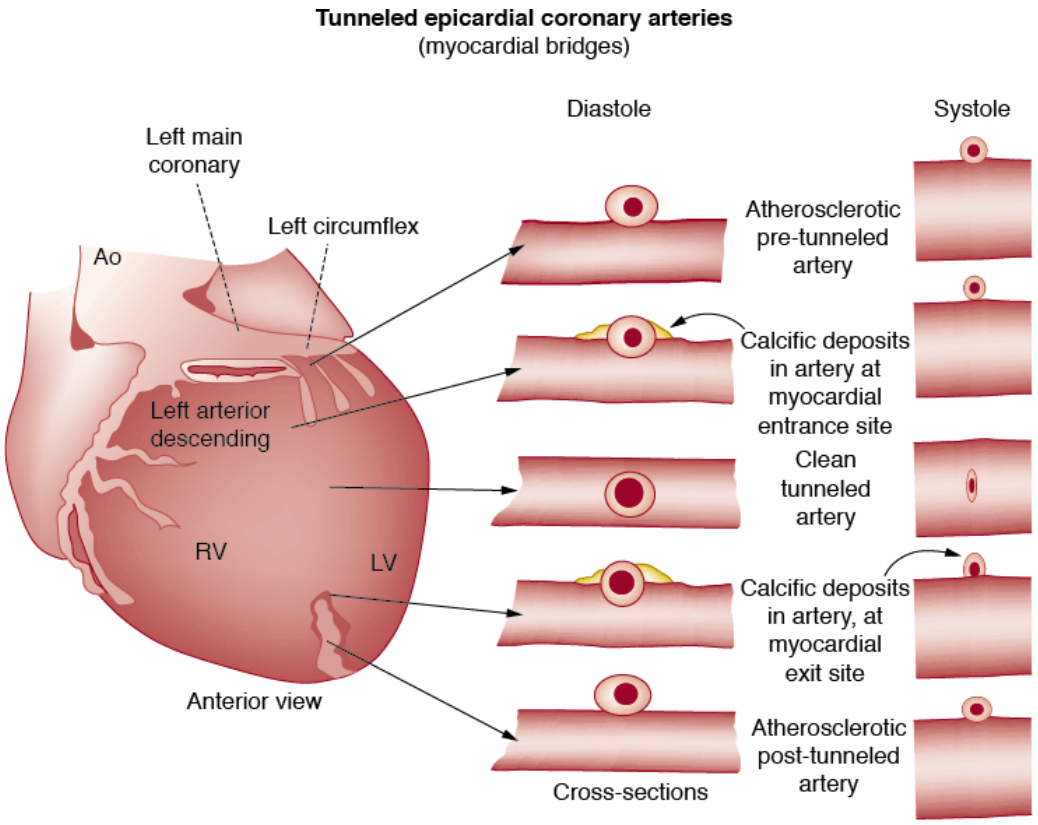




The above image shows how the penetrating myocardial branches of epicardial coronaries ramify to form the subendocardial arterial plexus and how they vary during systole and diastole.



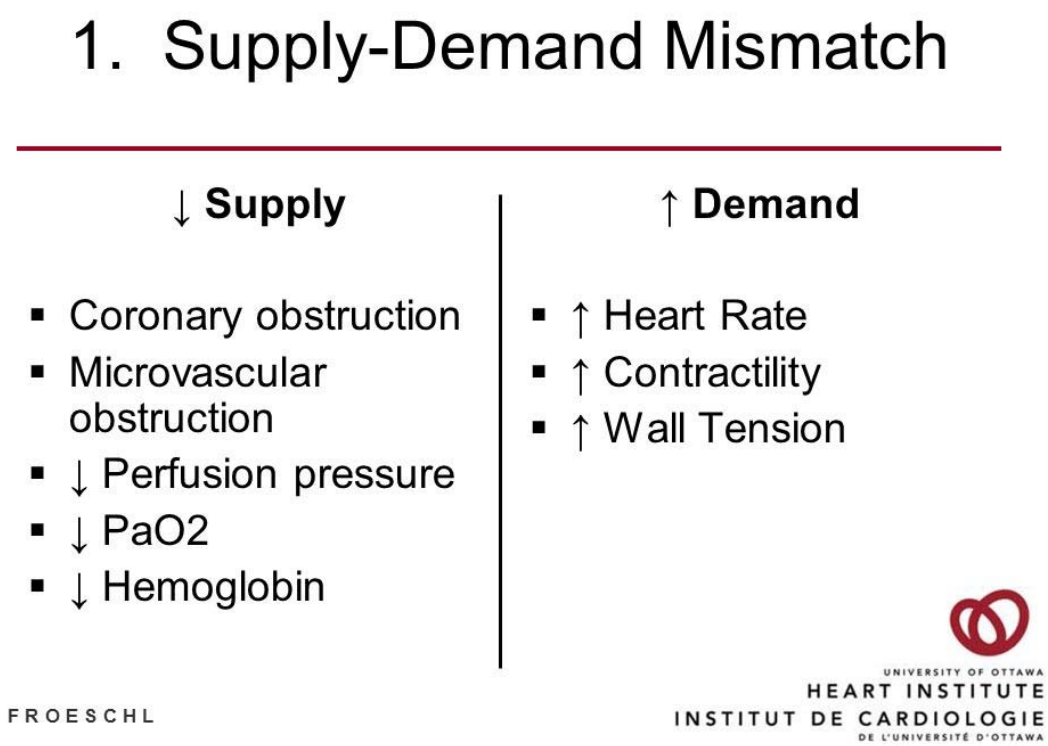
The above diagram shows the normal epicardial coronaries.



This image shows how the calibre of an intramural penetrating branch alters during systole and diastole.

MYOCARDIAL ISCHEMIA

Myocardial ischemia occurs when there is a mismatch between myocardial oxygen demand and supply.



Acute myocardial ischemia results in acute chest pain.

The causes leading onto an acute myocardial ischemia can be classified under the following headings:[16]

- CORONARY CAUSES
- NON CORONARY, CARDIAC CAUSES
- EXTRA CARDIAC CAUSES.

CORONARY CAUSES OF ACUTE MYOCARDIAL ISCHEMIA:

- Plaque rupture/ erosion
- coronary vasospasm
- spontaneous coronary dissection
- microcirculatory defects

- coronary thrombosis (spontaneous)
- embolus in coronary vasculature

NON CORONARY, CARDIAC CAUSES OF ACUTE MYOCARDIAL ISCHEMIA:

- Myocarditis
- Takutsubo cardiomyopathy
- Other cardiomyopathies
- Cardiac trauma
- Tachyarryhthmias
- Cardiotoxic drugs

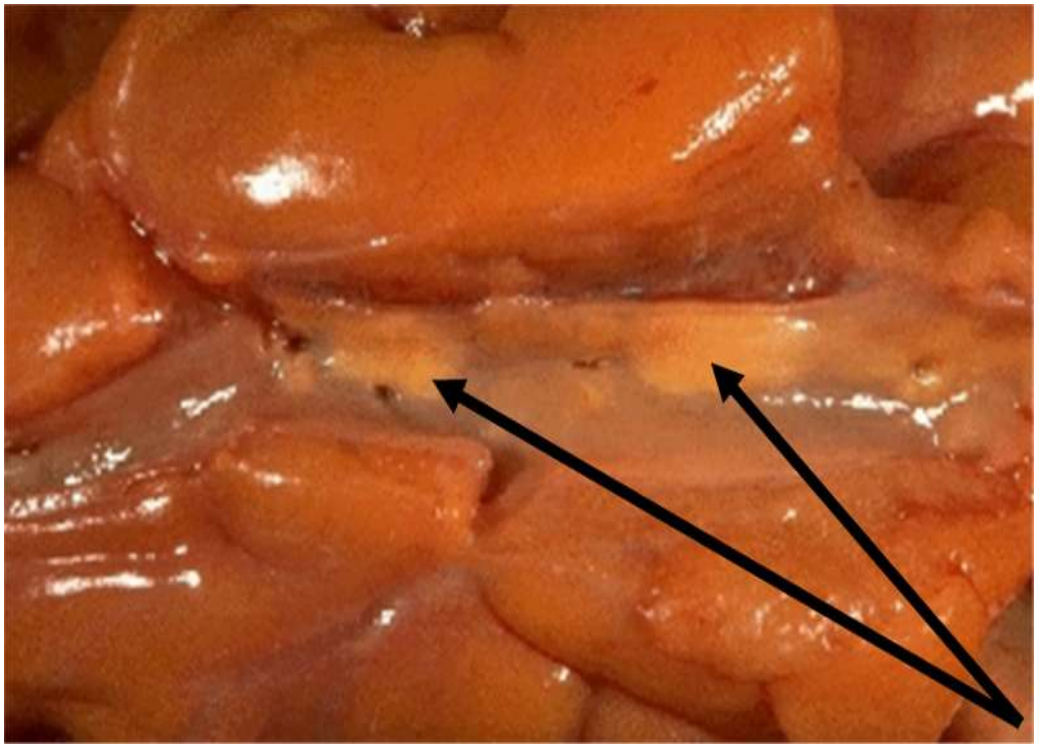
NON CARDIAC CAUSES OF ACUTE MYOCARDIAL ISCHEMIA:

- Pulmonary embolism
- Sepsis
- Adult Respiratory Distress Syndrome
- End Stage Renal Disease

Of all the above mentioned causes, rupture of atherosclerotic plaque is the commonest cause for acute myocardial ischemia presenting to the Emergency Room with acute onset chest pain.

ATHEROSCLEROTIC CORONARY ARTERY DISEASE:

The hardening of arterial vessel wall and deposition of lipids on the intimal surface of the vessel is called atherosclerosis. The process of genesis of atherosclerotic plaque starts in childhood when the consumption of pro atherosclerotic diet like diet rich in cholesterol and saturated fats begins[15]. The initial deposition causes a yellowish raise on the intima and is called the FATTY STREAK.



The arrows show the fatty streaks.

The traditional risk factors for atherosclerosis are the factors which actually promote inflammation, such as the following:

- Physical injury or stress on the endothelium due to direct trauma or hypertension

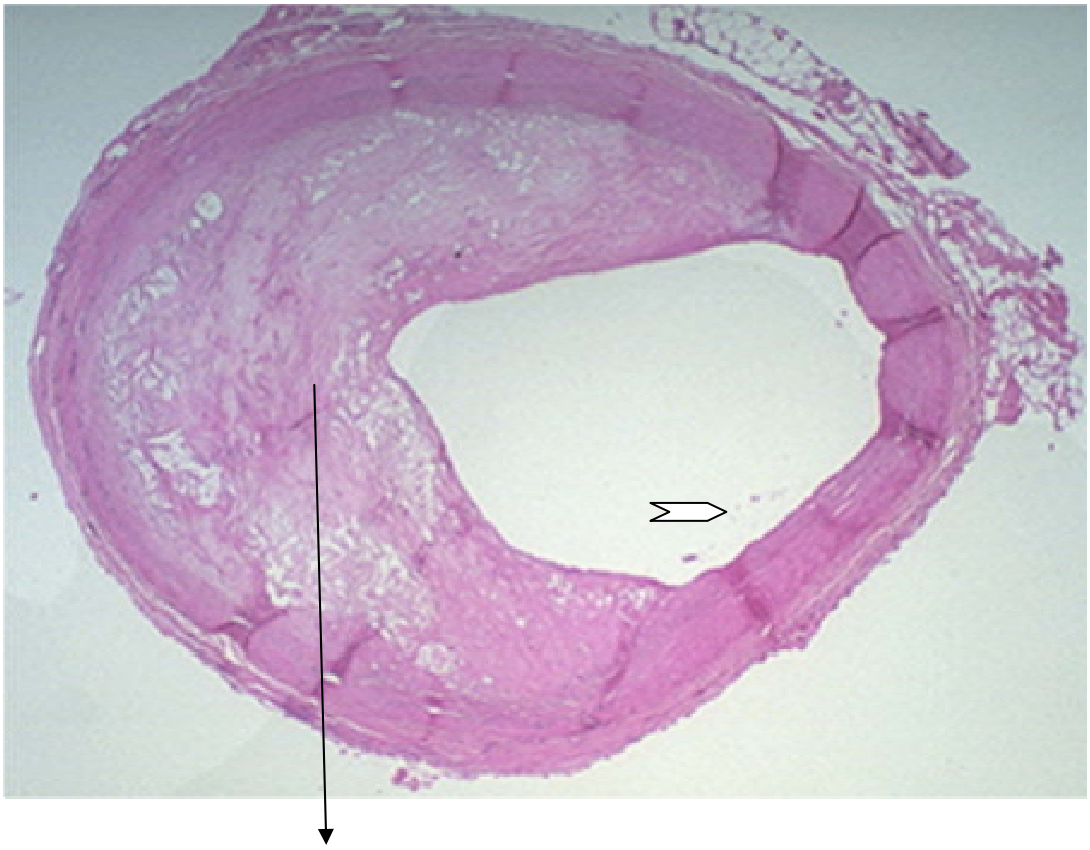
- Turbulence of blood flow, for example, where arteries branch
- Reactive oxygen species (free radicals), e.g., from smoking or air pollutants
- Hyperlipidemia (high blood concentrations of LDL or VLDL)
- Chronically elevated blood glucose levels
- Homocysteinemia, which results from an inherited metabolic defect that leads to very high levels of the homocysteine, a metabolite of methionine; high concentrations are toxic to the endothelium.

At the site of sheer stress and turbulence, lipoprotein molecules get adherent to the proteoglycan layer of the intimal endothelium and deposit in the intimal tunic. Owing to inflammation, the lipoprotein get modified by oxidation and glycation.

The modified lipoprotein further induces oxidative stress by inducing proinflammatory cytokine release which further aggravates local inflammation.

The expression of proinflammatory cytokines promotes the expression of cell adhesion molecules on the endothelium and recruits macrophages and other cells of inflammation.

The macrophages engulf the lipid molecules and such macrophage are called foam cells. Fibroblasts also home to the region of atherosclerosis and form a cap surrounding the lipid rich core.



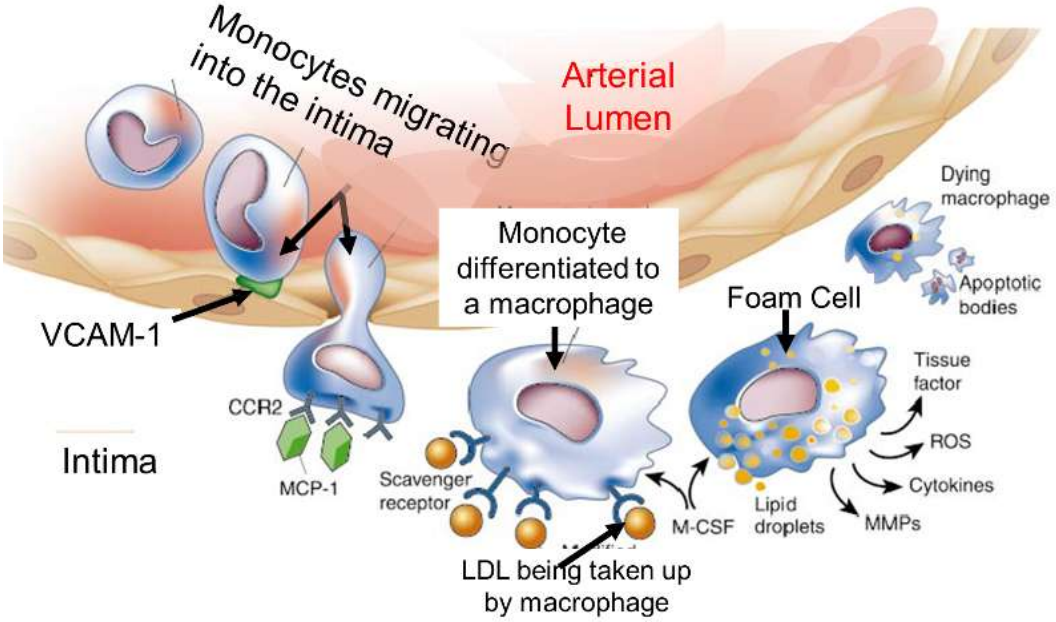
Arrow shows the plaque. Slit arrow head is the vessel lumen.

A LOW POWER HISTOPATHOLOGICAL IMAGE OF AN ATHEROSCLEROTIC PLAQUE

This takes place over many years and in this current era, the presence of atherosclerosis is ubiquitous albeit not all of those becoming symptomatic.

This lipid rich necrotic core with inflammatory cells covered by a layer of fibrous cap is called the atheroma and this obstructs the luminal calibre partially.

If the fibrous cap is thick, it means that the plaque is stable and if the fibrous cap is thin, then it may be prone for erosion or rupture and such plaques are called vulnerable plaques.



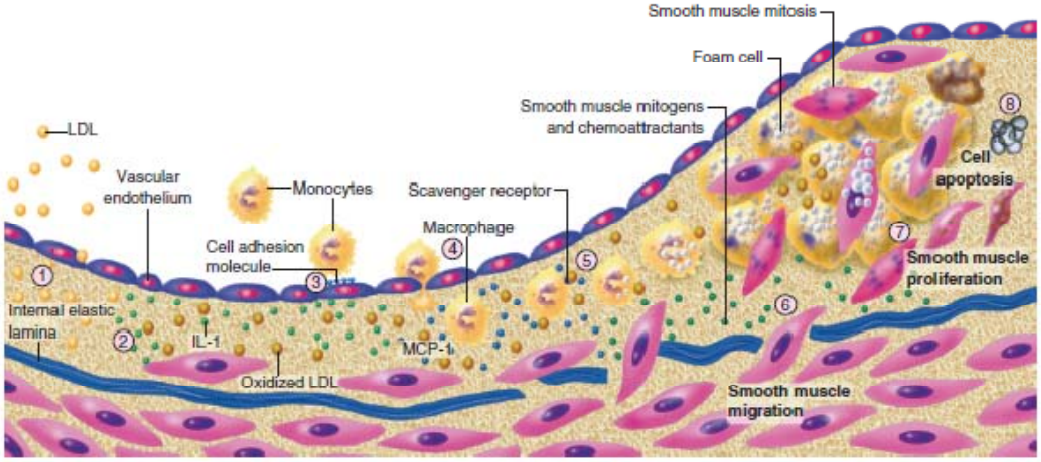
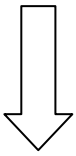


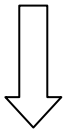
FIGURE 41-6 Schematic of the evolution of the atherosclerotic plaque. *1*, Accumulation of lipoprotein particles in the intima (*yellow spheres*). The modification of these lipoproteins is depicted by the *darker color*. Modifications include oxidation and glycation. *2*, Oxidative stress, including products found in modified lipoproteins, can induce local cytokine elaboration (*green spheres*). *3*, The cytokines thus induced increase expression of adhesion molecules (*blue stalks on endothelial surface*) for leukocytes that cause their attachment and chemoattractant molecules that direct their migration into the intima. *4*, Blood monocytes, on entering the artery wall in response to chemoattractant cytokines such as monocyte chemoattractant protein 1 (MCP-1), encounter stimuli such as macrophage colony-stimulating factor that can augment their expression of scavenger receptors. *5*, Scavenger receptors mediate the uptake of modified lipoprotein particles and promote the development of foam cells. Macrophage foam cells are a source of mediators, such as additional cytokines and effector molecules such as hypochlorous acid, superoxide anion (O_2^-), and matrix metalloproteinases. *6*, SMCs migrate into the intima from the media. *7*, SMCs can then divide and elaborate extracellular matrix, promoting extracellular matrix accumulation in the growing atherosclerotic plaque. In this manner, the fatty streak can evolve into a fibrofatty lesion. *8*, In later stages, calcification can occur (*not depicted*) and fibrosis continues, sometimes accompanied by SMC death (including programmed cell death or apoptosis), yielding a relatively acellular fibrous capsule surrounding a lipid-rich core that also may contain dying or dead cells and their detritus. IL = interleukin; LDL = low-density lipoprotein.

This diagram shows a schematic representation of the development of atherosclerotic plaque:

1. Low density Lipoproteins getting deposited in the tunica intima

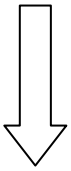


2. Darker molecules show LDL molecules that are modified by oxidation or glycation

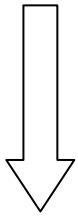


3. The green molecules are the proinflammatory cytokines the expression of which is induced by the oxidative stress created by the modified lipoproteins. These cytokines act as chemotactic factors for monocytes and induce the expression of cell adhesion molecules on the endothelium. This stage in the picture shows the margination of circulating monocytes aided by the pro inflammatory cytokine induced expression of cell adhesion molecules.

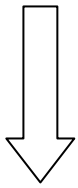
4. Shows diapedesis of the monocyte into the tunica intima.



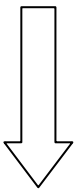
5. Activation of monocytes to macrophages, wherein they express scavenger receptors that aid in phagocytosis of the modified lipoprotein molecules by the macrophages. The lipid laden macrophages are called as FOAM CELLS.



6. The foam cells elaborate a lot of reactive oxygen and reactive nitrogen species and many other chemotactic molecules, causing migration of the smooth muscle cells from the tunica media into tunica intima.



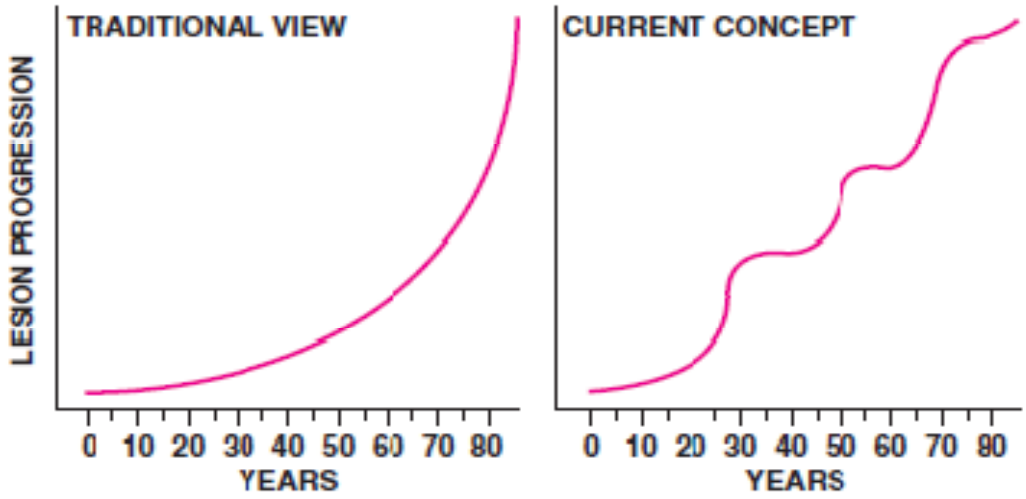
7. The smooth muscle cells proliferate and cause deposition of Extracellular matrix, and hence the fatty streak is not converted to fibrofatty atherosclerotic plaque.



8. The cells within the atherosclerotic plaque undergo necrosis and apoptosis and there occurs calcium deposition in the plaque. As the plaque grows in size, angiogenesis occurs to the plaque and the newly formed blood vessels are friable like that of the neovessels formed in a diabetic retina.

The deposition of lipid starts early in life and the rate of progression or growth of the atherosclerotic plaque depends on the presence of the classical risk factors for atherosclerosis, which all aid in maintaining a proinflammatory state.

THE GROWTH OF THE ATHEROSCLEROTIC PLAQUE:



The above graphs depict the pattern of atherosclerotic plaque growth. The age old concept as depicted by the graph on the left was that the atheromatous plaque once formed, the rate of its growth is uniformly progressive with the age.

The recent concept is that, the growth of atherosclerotic plaque is not uniform. It shows a serpentine or a stepladder type of growth rather than a smoothly progressive curve. That is the as the plaque grows, its growth may fall into a quiescence phase owing to factors like plaque rupture or plaque hemorrhage, which may or may not be clinically significant.

CORONARY ATHEROSCLEROSIS:

Atherosclerotic plaques even though if present, they can be asymptomatic. There came the concept of **SIGNIFICANT Coronary atherosclerotic disease,** which is defines based on Coronary Angiogram features.

Significant coronary atherosclerosis is defined as the[29],

- presence of plaque occluding 50% or more in Left Main Stem artery
- plaque occluding 70% or more of the lumen of other major coronary vessel
- plaque occluding 30-70% of the lumen with a Fractional Flow Reserve (FFR) of ≤ 0.8.

Fractional flow reserve is the ratio of the intraluminal pressure distal to the stenosis to the intraluminal pressure proximal to the stenosis.

Angiographic guide wire with pressure sensor is used to measure pressure proximal and distal to the stenosis.

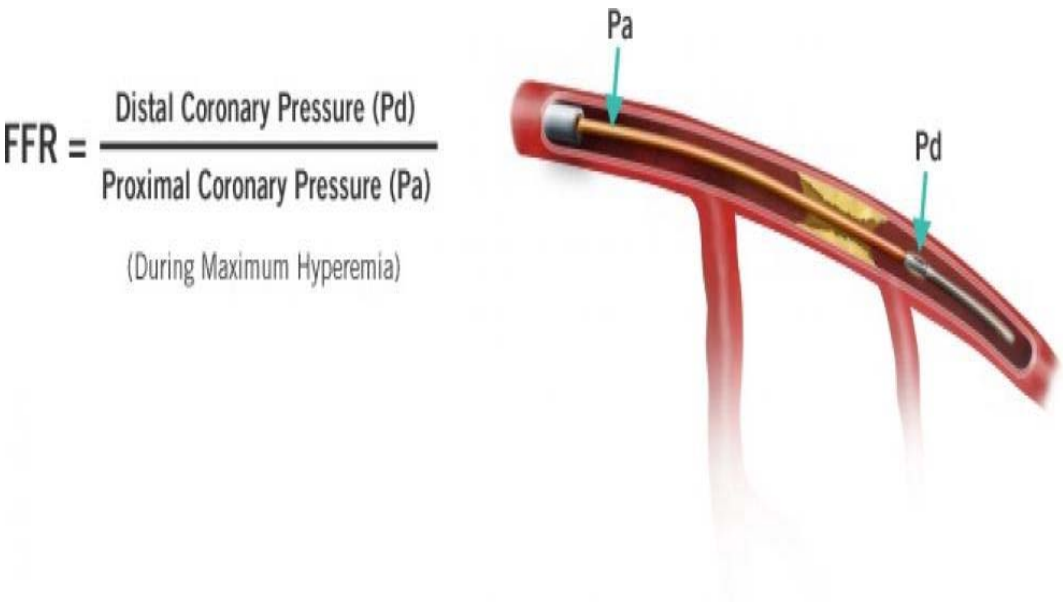
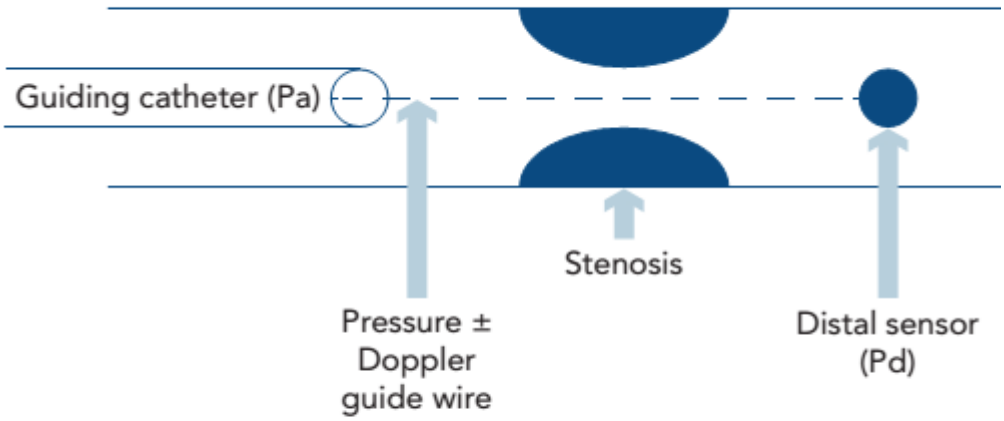


Figure 1: Schematic of the Method Used to Measure Fractional Flow Reserve in the Catheterisation Laboratory



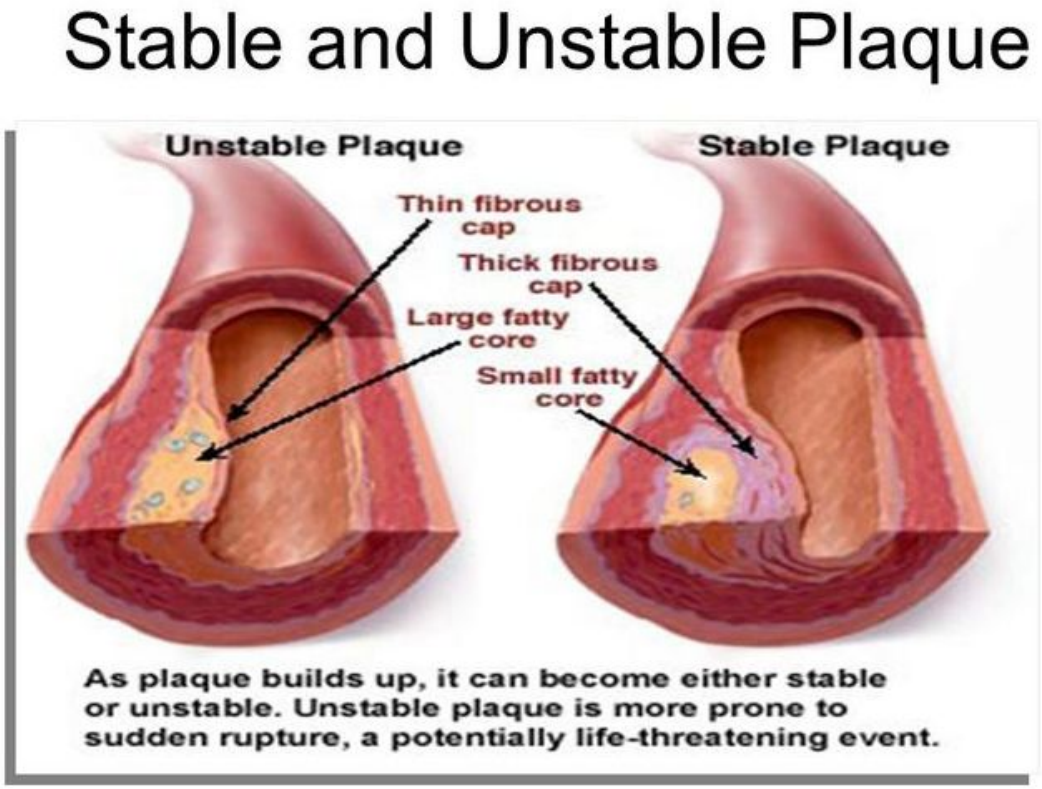
Concomitant measurement of aortic pressure (Pa) and coronary pressure (Pd) across a coronary stenosis is performed at rest and maximal vasodilatation obtained by the administration of different drugs (e.g. adenosine/ATP [intravenous: 140 µg/kg/min; intracoronary: 50–150 µg]; papaverine [right coronary artery: 12–6 mg; left coronary artery: 16–20 mg]; nitroprusside [intracoronary bolus: 0.6 µg/kg]) to establish fractional flow reserve in the catheter laboratory. Normal fractional flow reserve is Pd/Pa greater than 0.75 at maximal hyperaemia.

STABLE AND VULNERABLE PLAQUES:

Post mortem studies in patients who had fatal myocardial infarction have revealed that their atherosclerotic plaques had a common feature. There evolved the concept of stable and vulnerable atherosclerotic plaques.

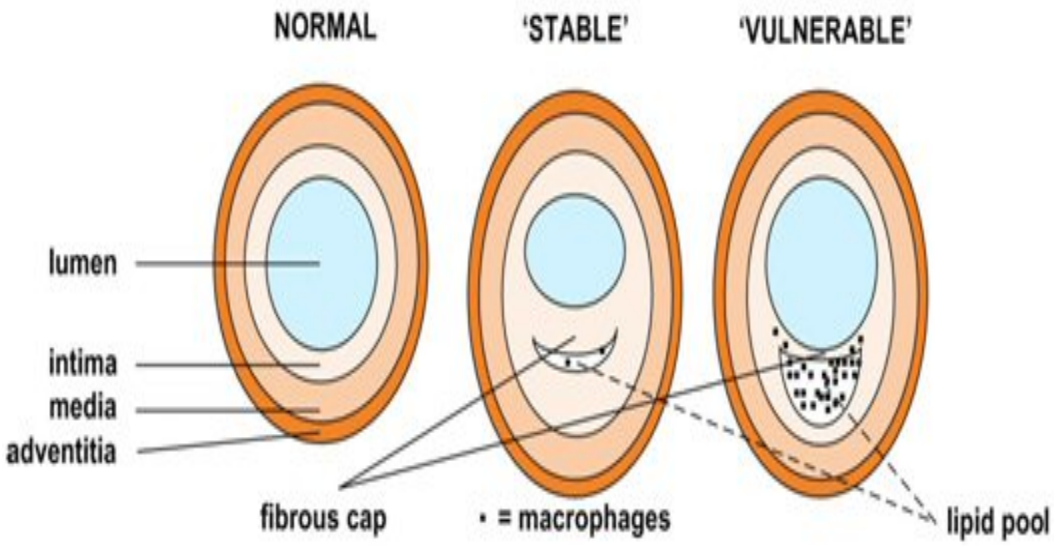
Stable plaques are those plaques that are covered by a thick fibrous cap on their luminal side. Vulnerable plaques are those plaques that are covered by a thin fibrous cap overlying a dense lipid core that is necrotic.

The thin fibrous cap is prone for rupture thereby exposing the prothrombotic lipid core and hence called as vulnerable plaque[19].



Various methods have been introduced and studied to study the characteristics of a plaque such as Intravascular ultrasonography, Optical Coherence Tomography, CT Coronary Angiography and MRI.

CLINICAL MANIFESTATIONS OF SIGNIFICANT CORONARY ATHEROSCLEROTIC DISEASE:



STABLE ANGINA

Patients with significant coronary atherosclerosis can walk around asymptomatically also.

Some patients with a stable plaque, may be asymptomatic at rest, as the reduced blood flow occurring despite the plaque may be sufficient to meet the oxygen demands of the myocardium at rest.

But in situations where the myocardial oxygen demand increases such as during exercise, the fixed plaque leading to a decreased coronary blood flow would not be sufficient in meeting the increased oxygen demand. So there occurs myocardial ischemia that leads onto the patient experiencing anginal pain.

But once the myocardial oxygen demand decreases as when the patient stops exercising, the adequacy of blood supply now to the myocardium matches the oxygen demand and the angina gets relieved.

This is a **DEMAND LED ISCHEMIA due to a fixed STABLE plaque** and this syndrome is called **STABLE ANGINA.** It is a clinical syndrome and the ECG remains normal and there is no Troponinaemia.

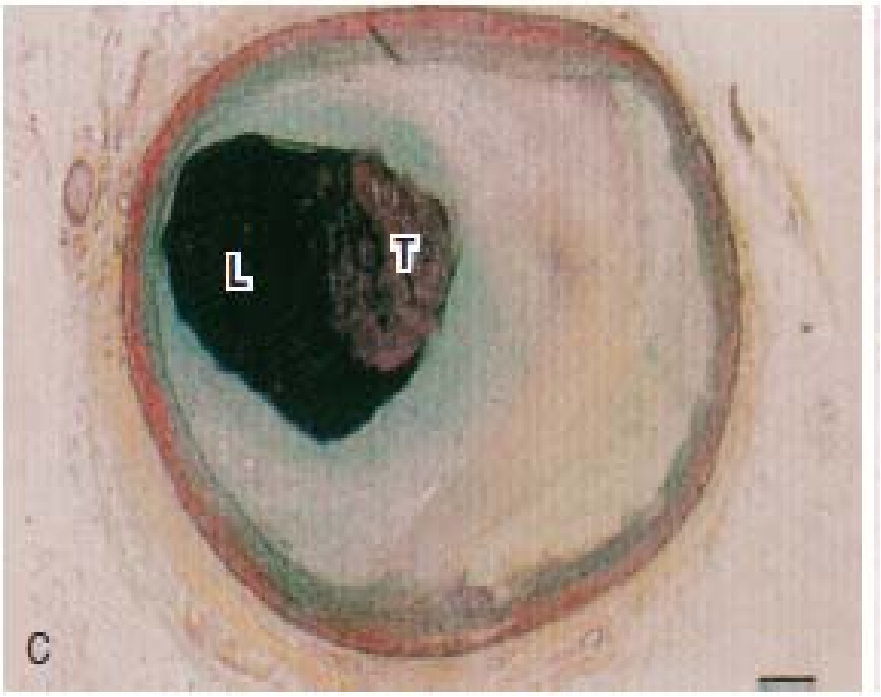
UNSTABLE CORONARY SYNDROMES

An unstable or vulnerable plaque may undergo plaque rupture, which is the rupture of the fibrous cap, or may undergo erosion of the overlying endothelium, thus exposing the underlying necrotic lipd core which is prothrombotic, thus setting off the coagulation cascade leading to the formation of platelet plug quickly followed by a thrombus at the site of catastrophe.

A rapidly forming thrombus increases and occludes the lumen progressively, thereby causing an **abrupt decrease in blood SUPPLY to the myocardium,** leading to ischemia of the myocardium which presents as pain occurring at rest or that which started during exertion but not relieved by rest.

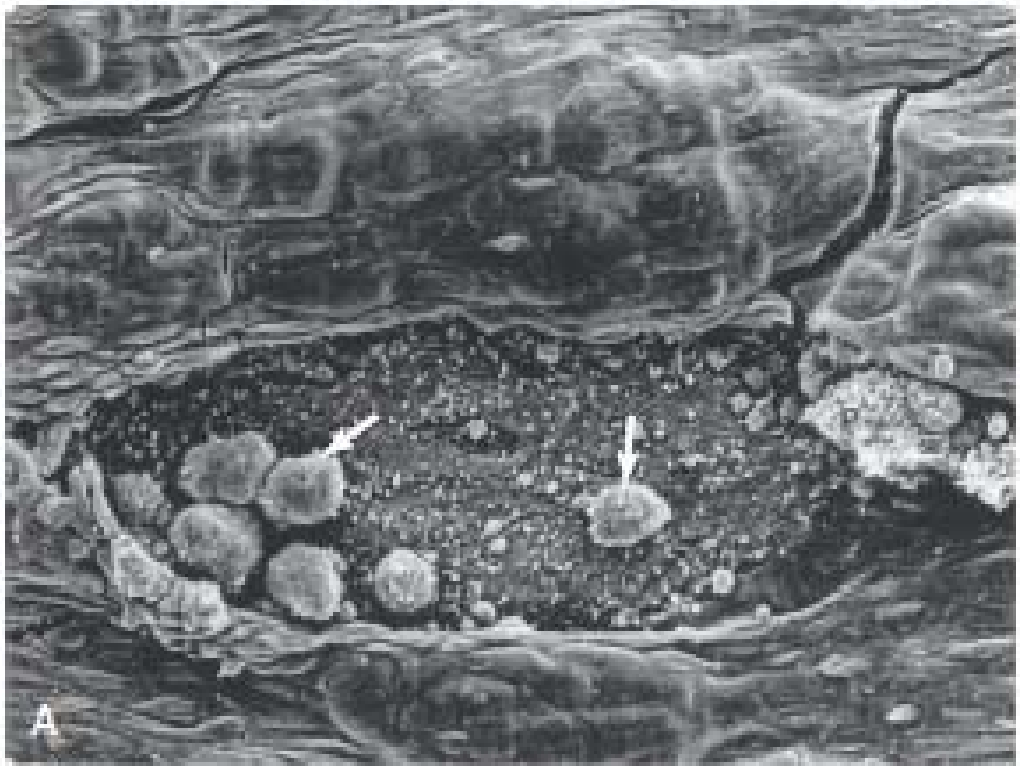
This is **SUPPLY LED ISCHEMIA, due to a ruptured or eroded unstable plaque.**

THIS IS ACUTE CORONARY SYNDROME

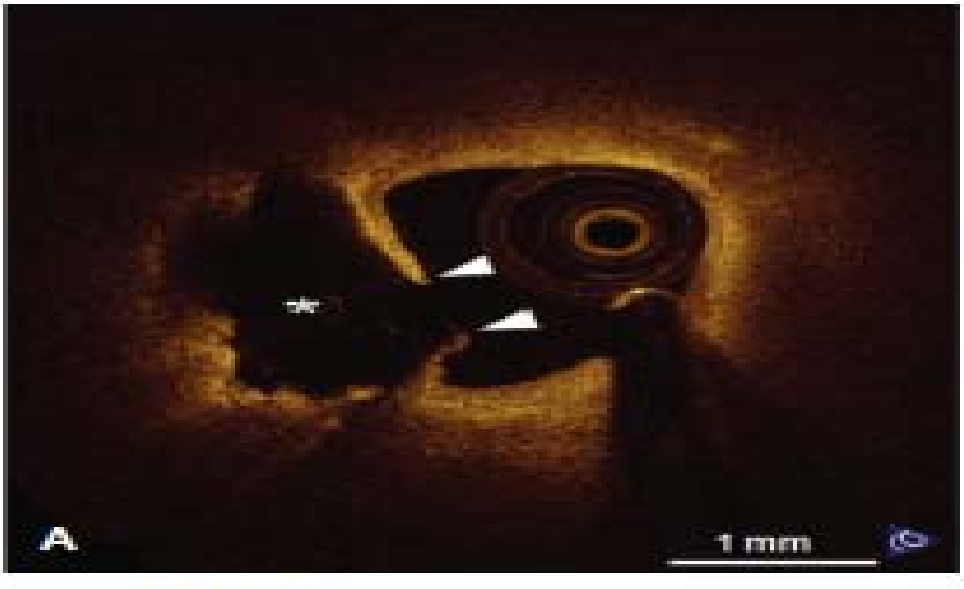


The image above is a low power histopathological section of coronary arterial thrombus that had occurred following plaque erosion.

The image below shows a Scanning Electron Microscopy image of superficial plaque erosion, exposing the subendothelium. The arrow marks show the leucocytes that have started to adhere to the denuded surface.

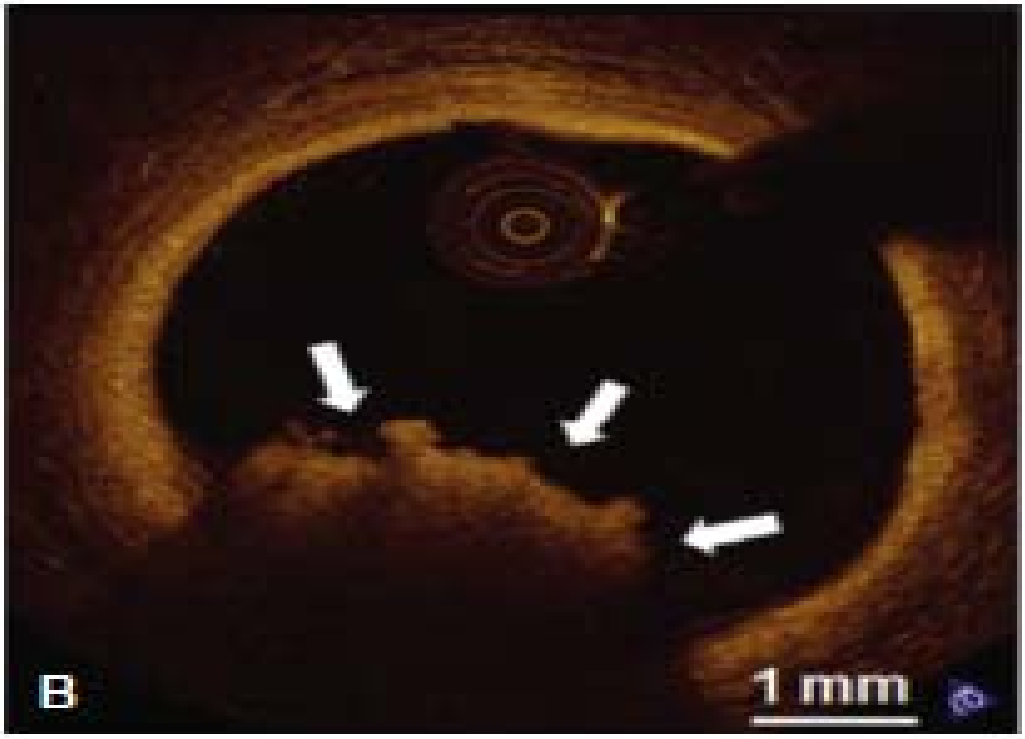


The image shown below is Optical Coherence Tomography image of plaque rupture. The arrow heads mark the endothelial discontinuity.[30]



The asterisk represents the lipid rich core of the plaque.

The image below is Optical Coherence Tomography image of a thrombus that had formed over the ulcer created by plaque rupture.



Arrows show the thrombus.

Plaque rupture is responsible for 75% of the Acute Coronary Syndromes and is more common in men, whereas Plaque erosion is commoner in ACS occurring in women less than 50 years of age. But Plaque rupture predominates the cause leading to ACS in older women.

The plaque characteristics of a vulnerable plaque that could lead onto an ACS have been studied. The following are the morphological characteristics of dangerous plaques:[18,19]

- Lipid burden >70%
- Thin fibrous cap

- Causing a luminal area of 4 mm sq. or lesser
- Expansive remodelling which stretches and thins out the fibrous cap and minimizing luminal obstruction, leading to a misleadingly mild stenosis on coronary angiography.
- Plaque hemorrhage
- Neovascularisation
- Spotty pattern of calcification
- Adventitial inflammation.

An acute increase in inflammatory burden could precipitate a plaque rupture, as inflammation leads to overexpression of enzymes that degrade the plaques extracellular matrix. This is the reason behind vaccinating people with high risk coronary artery disease risk with Pneumococcal and Influenza vaccinations as an episode of these infections could result in an acute increase in the inflammatory burden leading onto plaque rupture, thereby precipitating an acute coronary syndrome.

Other factors leading to plaque rupture are

- Stress induced by intraluminal pressure
- Tachycardia (cyclical stretching and compression)
- Coronary vasomotor tone.

Many physiologic parameters namely systolic blood pressure, heart rate, blood viscosity, plasminogen activator inhibitor-1 (PAI-1) level, plasma cortisol levels, and plasma epinephrine levels exhibit circadian and seasonal

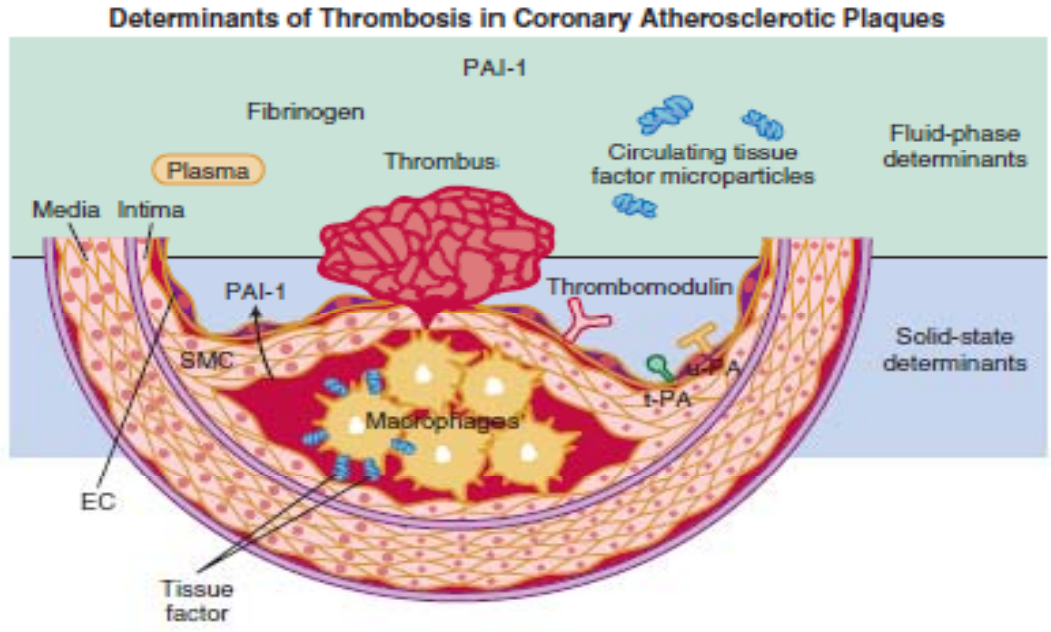
variations and increase at times of stress. These factors act in concert to heighten the propensity for plaque disruption and coronary thrombosis, with the result that STEMI clusters in the early morning hours, especially in the winter and after natural disasters[21-23]

Not all plaque ruptures or erosions will lead onto the formation of a thrombus that progresses to occlude the lumen completely. What determined the thrombus size can be classified into the factors in the blood and factors in the lipid plaque per se, which are grouped as

- Fluid phase determinants
- Solid state determinants.

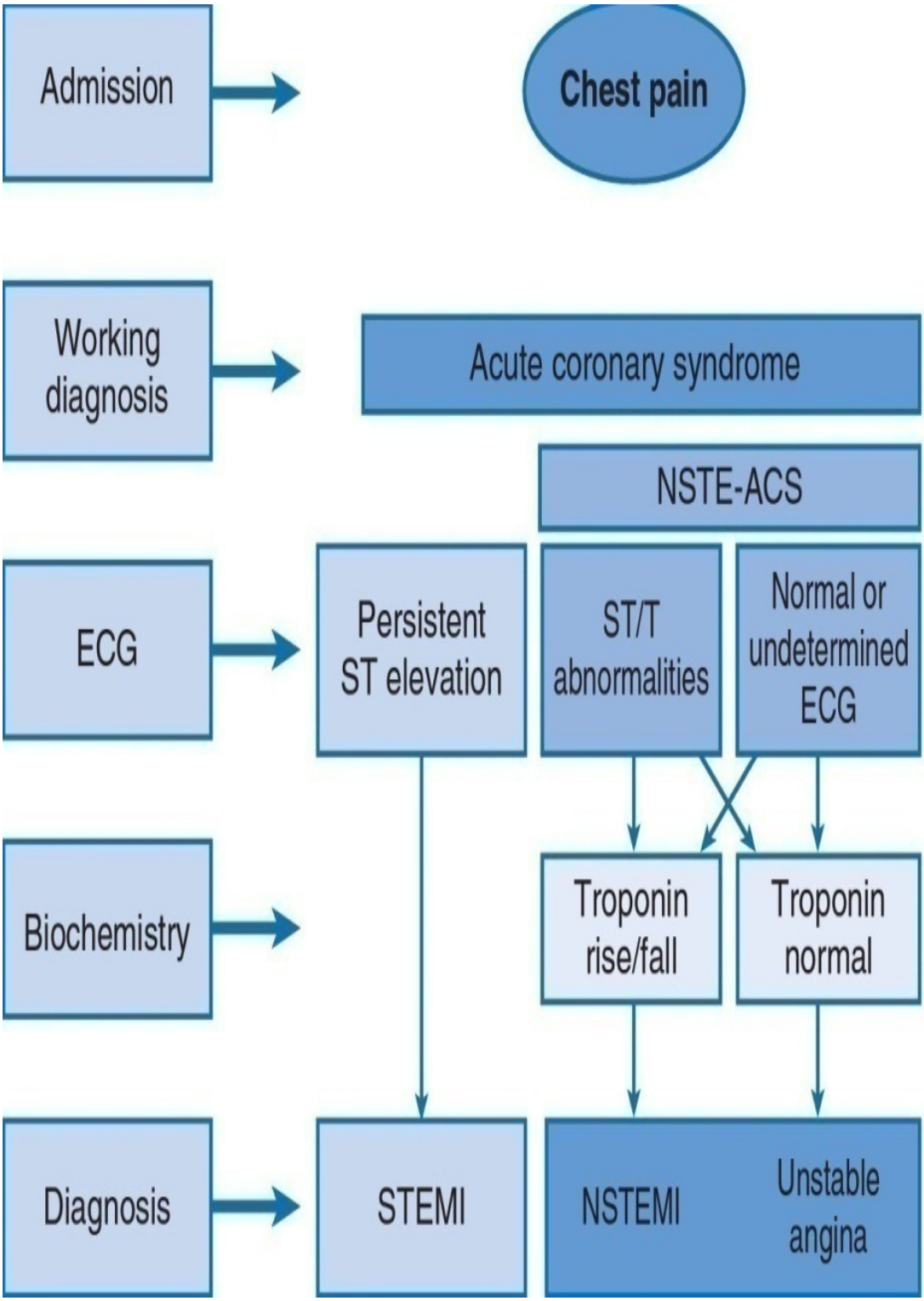
The following schematic represents the two state model of atherothrombosis. The vulnerable plaque has a thin fibrous cap covering a large lipid core that contains abundant tissue factor–bearing macrophages. When the fibrous cap ruptures, pro coagulant proteins in the fluid phase of blood gain contact with tissue factor–bearing macrophages and microparticles derived from apoptotic cells present in the solid state of the plaque. These events trigger thrombus formation on the ruptured plaque. The consequences depend on the amount of tissue factor and apoptosis in the plaque's core and on the levels of fibrinogen and Plasminogen Activator Inhibitor-1 in the blood. This interaction of the fluid phase with the solid state will determine whether a given plaque disruption provokes a partial or transient coronary artery occlusion (that can be clinically silent or less commonly cause an episode of

unstable angina) or a devastating persistent and an occlusive thrombus that can lead to an acute myocardial infarction. Inflammation regulates the thrombotic/fibrinolytic balance in both the solid state and the fluid phase, because PAI-1 and fibrinogen both are acute-phase reactants and because the inflammatory mediator CD40 ligand (CD154) induces tissue factor expression.



The fate of rupture of vulnerable plaque is an Acute Coronary Syndrome, which depending upon the fluid phase and solid state determinants has the size of thrombus causing an episode of Unstable Angina or going on to lead onto myocardial infarction namely Non ST Elevation or ST Elevation myocardial infarction.

ACUTE CORONARY SYNDROME



An Acute Coronary Syndrome occurs when the coronary blood flow is reduced suddenly and severely due to atherothrombus plaque rupture/The myocardium supplied by the occluded artery will immediately become ischemic. If blood flow is not restored rapidly, the ischemic area will undergo infarction(necrosis) which leads to irreversible cell death. The infarction will commence in the most ischemic area and from there it will gradually expand.

If the artery is completely occluded, all ischemic myocardium will be dead in 2 to 12 hours. The size of the ischemic or necrotic area correlates strongly with the risk of heart failure, malignant ventricular arrhythmias and other complications.

An Acute Coronary syndrome occurs when an atherosclerotic plaque disrupts, which results in activation of platelets and coagulation factors ultimately forming a thrombus, which occludes the artery.

The occlusion can be partial or complete depending upon the size of the thrombus and the plaque itself.

Acute Coronary Syndromes can be divided into ST Elevation ACS and Non ST Elevation ACS. ST Elevation ACS is the ST Elevation Myocardial Infarction called as STEMI where there is a transmural myocardial infarction leading onto the development of ST segment elevation on the ECG along with cardiac biomarker positivity, the diagnosis of which is not difficult owing to the typical ECG patterns defined in the 3^{RD} and 4^{TH} UNIVERSAL DEFINITIONS OF MYOCARDIAL INFARCTION[6].

Definition of myocardial infarction

Criteria for acute myocardial infarction

The term acute myocardial infarction (MI) should be used when there is evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischaemia. Under these conditions any one of the following criteria meets the diagnosis for MI:

- Detection of a rise and/or fall of cardiac biomarker values [preferably cardiac troponin (cTn)] with at least one value above the 99th percentile upper reference limit (URL) and with at least one of the following:
  - Symptoms of ischaemia.
  - New or presumed new significant ST-segment–T wave (ST–T) changes or new left bundle branch block (LBBB).
  - Development of pathological Q waves in the ECG.
  - Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
  - Identification of an intracoronary thrombus by angiography or autopsy.
- Cardiac death with symptoms suggestive of myocardial ischaemia and presumed new ischaemic ECG changes or new LBBB, but death occurred before cardiac biomarkers were obtained, or before cardiac biomarker values would be increased.
- Percutaneous coronary intervention (PCI) related MI is arbitrarily defined by elevation of cTn values (>5 x 99th percentile URL) in patients with normal baseline values (≤99th percentile URL) or a rise of cTn values >20% if the baseline values are elevated and are stable or falling. In addition, either (i) symptoms suggestive of myocardial ischaemia or (ii) new ischaemic ECG changes or (iii) angiographic findings consistent with a procedural complication or (iv) imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality are required.
- Stent thrombosis associated with MI when detected by coronary angiography or autopsy in the setting of myocardial ischaemia and with a rise and/or fall of cardiac biomarker values with at least one value above the 99th percentile URL.
- Coronary artery bypass grafting (CABG) related MI is arbitrarily defined by elevation of cardiac biomarker values (>10 x 99th percentile URL) in patients with normal baseline cTn values (≤99th percentile URL). In addition, either (i) new pathological Q waves or new LBBB, or (ii) angiographic documented new graft or new native coronary artery occlusion, or (iii) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.

Criteria for prior myocardial infarction

Any one of the following criteria meets the diagnosis for prior MI:

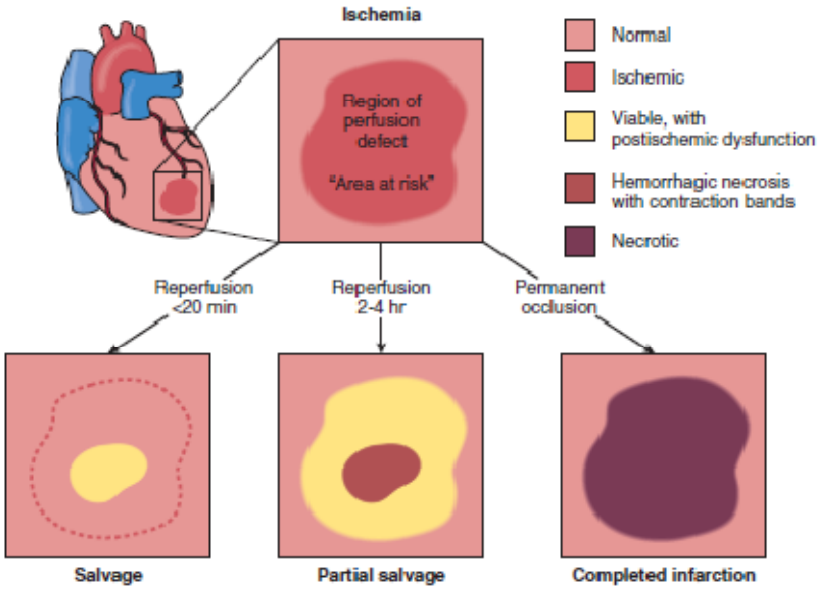
- Pathological Q waves with or without symptoms in the absence of non-ischaemic causes.
- Imaging evidence of a region of loss of viable myocardium that is thinned and fails to contract, in the absence of a non-ischaemic cause.
- Pathological findings of a prior MI.

The Non ST Elevation ACS include the Non ST Elevation Myocardial Infarction called as NSTEMI and Unstable Angina.

In NSTEMI, there is infarction leading to cardiac biomarker positivity but the infarct is not transmural and hence there is no ST segment elevation. But ECG shows other features of ischemia. On the other hand, in Unstable Angina, there is no infarction and hence cardiac biomarker negativity. ECG shows features of ischemia but again, not ST elevation.

As for STEMI, there is no clear definition framed for NSTE-ACS and if left untreated, around 50% of the patients may proceed on to have full blown STEMI.

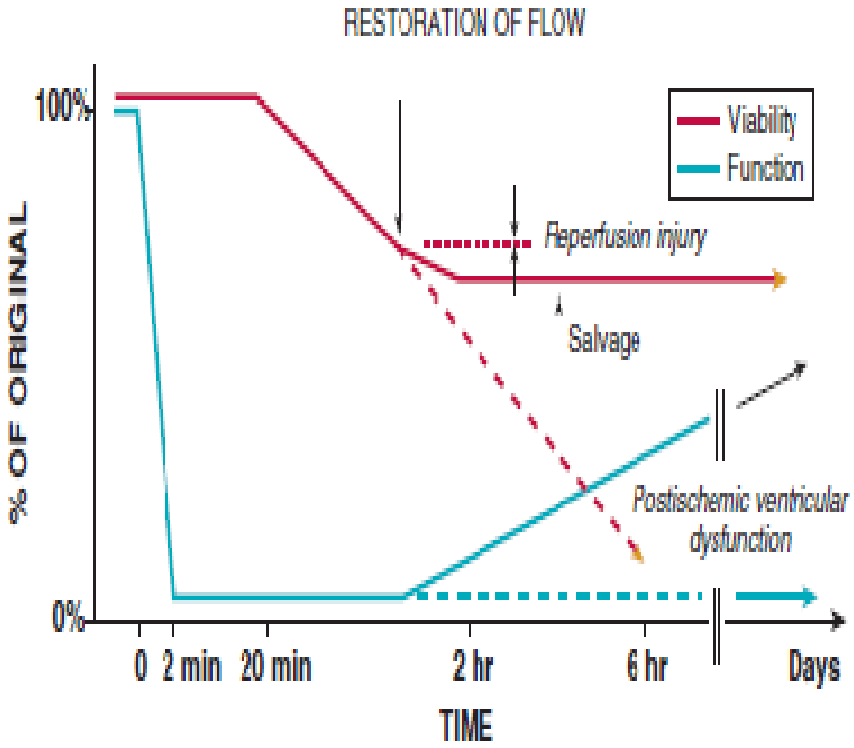
Hence timely recognition of NSTE-ACS is crucial. The significance of time is depicted in the image below:[12,13]



Hence when intervened on time, the progressive thrombus formation can be aborted, Infarction can be prevented and myocardium can be salvaged.

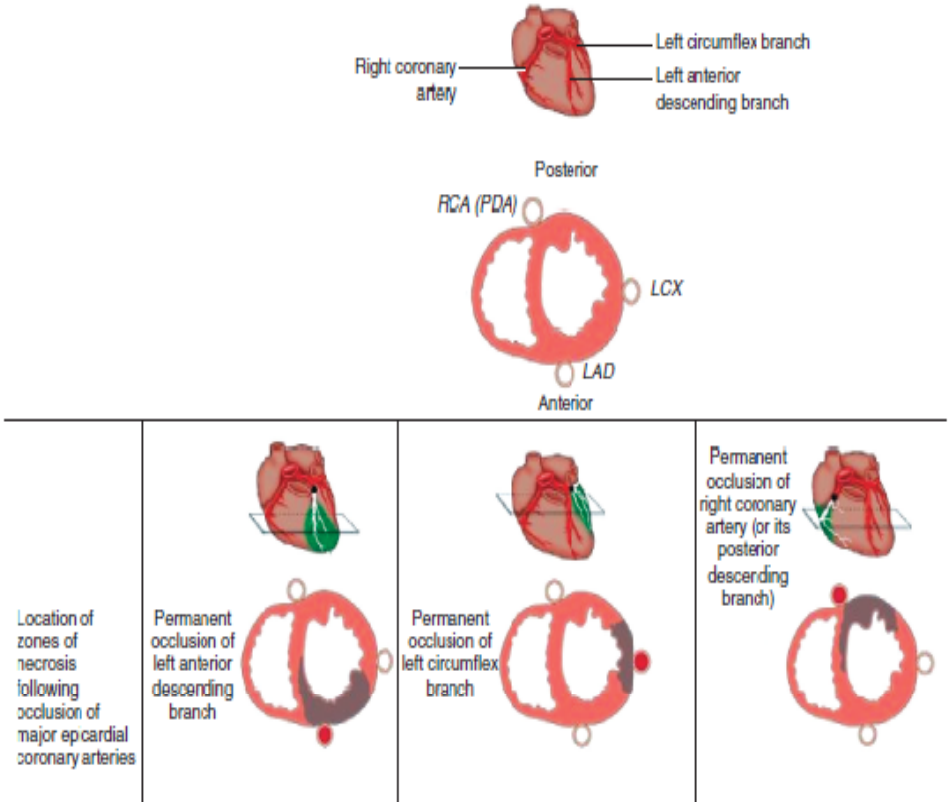
The representation above depicts the consequences of reperfusion at various times after coronary occlusion. In the above image, the mid portion of the left anterior descending coronary artery is occluded and a large zone of ischemic myocardium develops, called the “area at risk.” If Reperfusion occurs in less than 20 minutes, it does not result in permanent loss of tissue, but for a transient period of myocardial contractile dysfunction called “stunning”. If

reperfusion occurs later, it results in hemorrhagic necrosis with contraction bands. Permanent occlusion results in necrosis of myocardium.

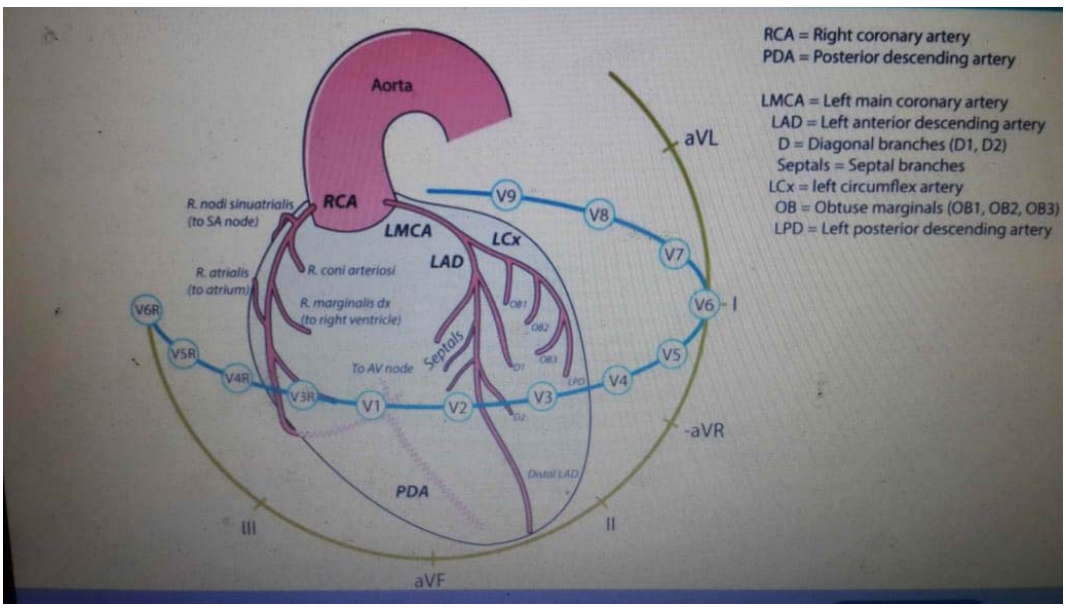


The importance of the above graph is that it depicts the importance of timely identification of Acute Coronary Syndrome. Though the myocardial function declines rapidly following ischemia (as depicted by the blue curve), The myocardium remains viable for a longer period (as depicted by the red curve) which can be salvaged if aggressively managed.

The following image shows the schematic representation of the three major epicardial coronaries and the areas subtended by their supply which are prone to ischemia or infarction if they are occluded.[14]

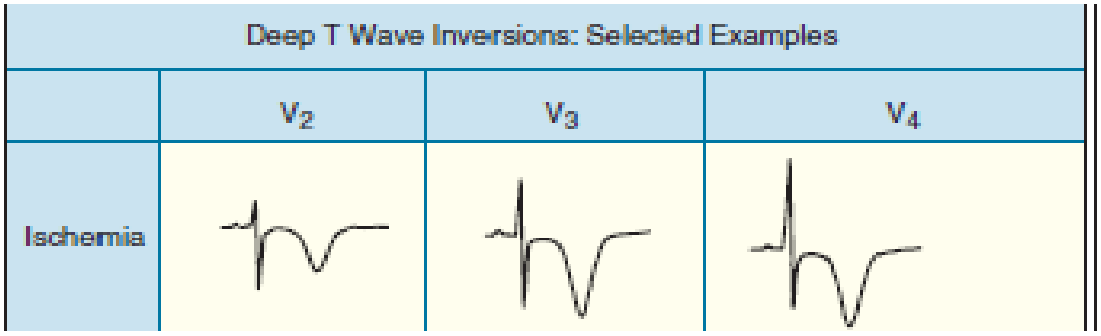


Electrocardiogram is a very useful basic diagnostic tool in the diagnosis of coronary artery disease, as the leads overlying specific regions of the heart pick up the ischemic changes occurring there giving us clue about the culprit artery .

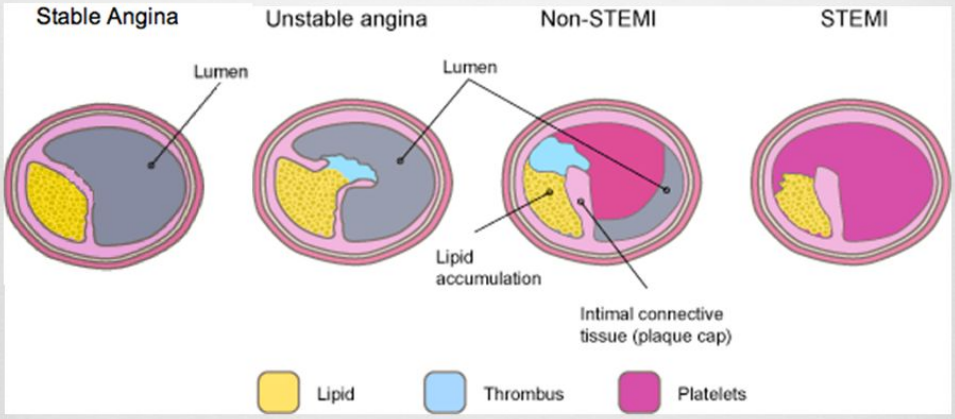


Localization	Leads (predominant)	Anatomy
ANTERIOR WALL		
'Extensive' anterior (anterior-lateral)	V_1–V_6, I, aVL	Proximal LAD occlusion
Septal	V_1–V_3(V_4)	Septal perforators of LAD
Anterior (localised or true)	V_4–V_6 (I, aVL, V_2)	Diagonal (supplies anterior LV wall). Occasionally marginal branches of Cx
Lateral (apical)	V_5, V_6 I, aVL	Distal LAD or circumflex
INFERIOR WALL		
Inferior (localized)	II, III, aVF	RCA or posterolateral branch of Cx
Inferior (extended)	II, III, aVF plus	
Infero-lateral	I, aVL, V_5, V_6	RCA or dominant Cx
Infero-posterior*	V_1–V_2	Posterior descending branch or RCA or posterolateral branch of Cx
Right ventricular	V_1, V_3R, V_4R (additional right chest leads helpful)	Proximal RCA occlusion

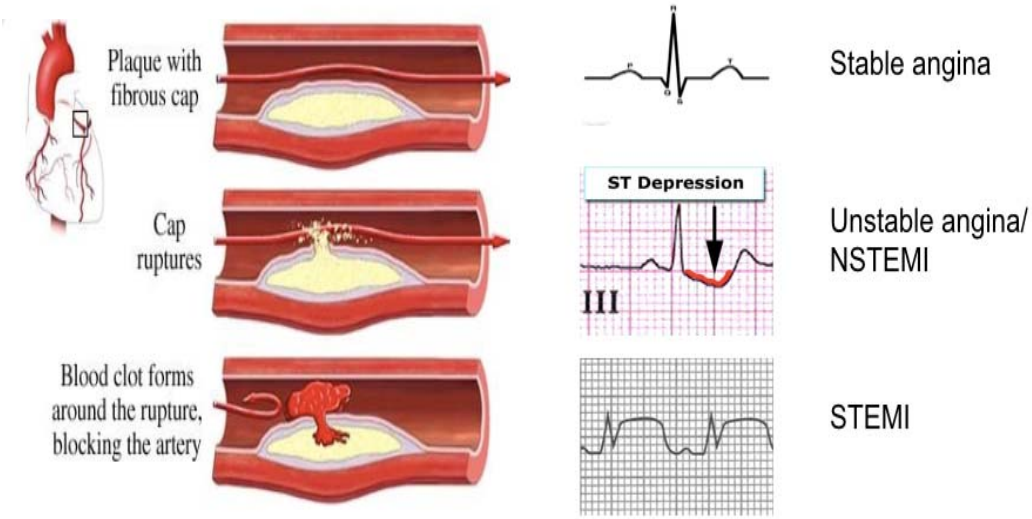
The ischemic T wave inversions:



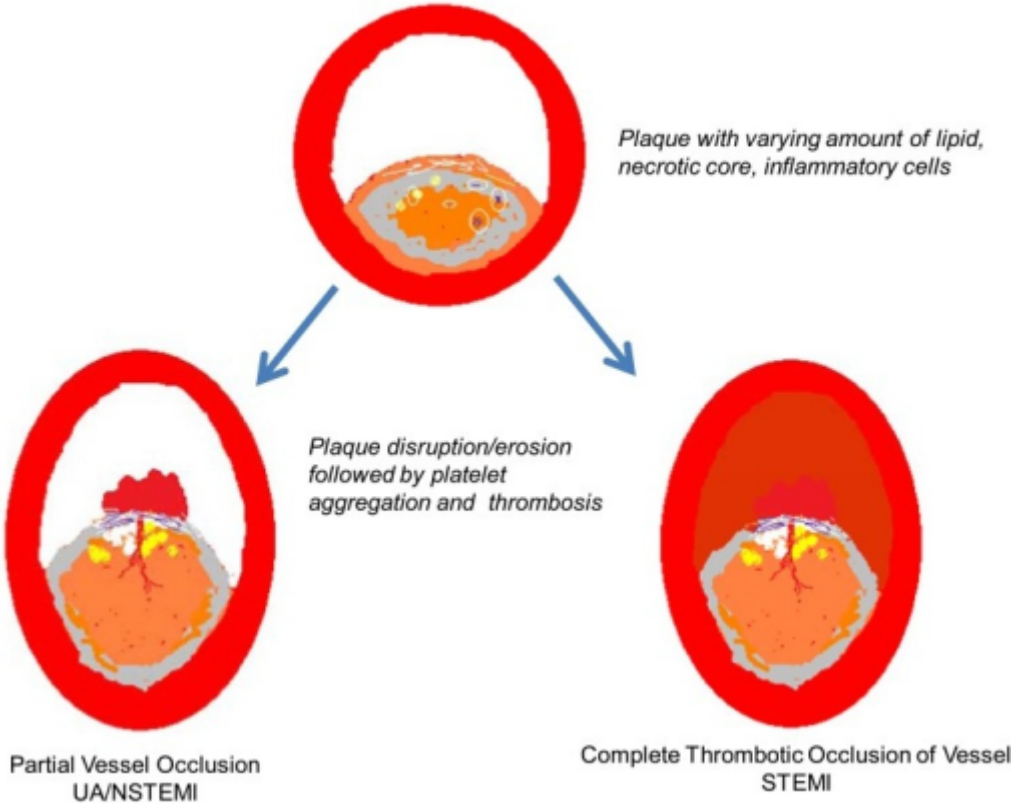
Terminology

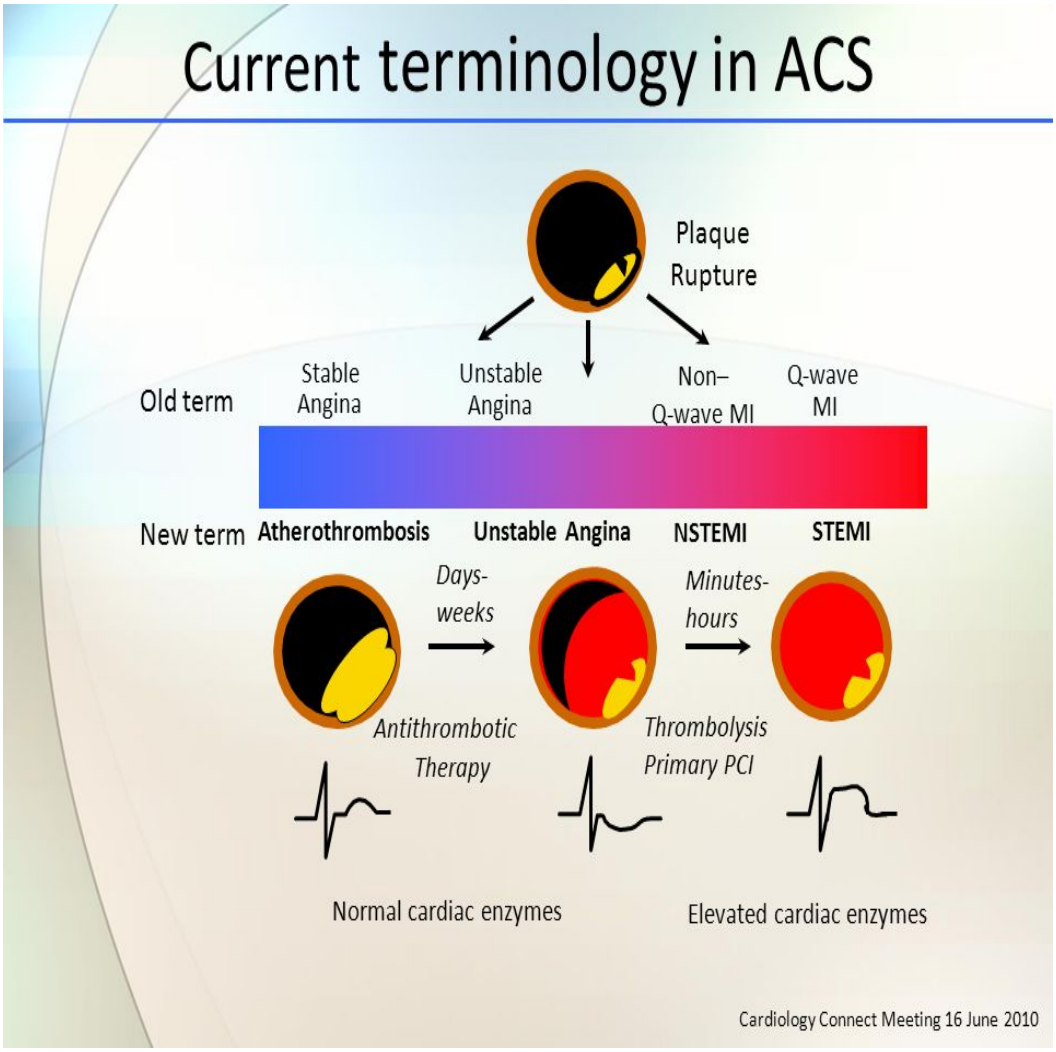


Coronary Atherosclerosis: Vascular Biology



Atherosclerosis: Progression to ACS





CARDIAC TROPONINS:

Cardiac Troponins are the preferred biomarker to detect myocardial injury. They are present within the myocyte, enclosed by the intact sarcolemma. In conditions of myocyte injury, the ensuing sarcolemmal disruption leads to these intracellular molecules shed into the circulation.

The presence of Cardiac Troponins in the general circulation, called Troponinaemia, signifies myocardiocyte disruption or injury, whatever be the cause[24-25].

Myocyte necrosis due to infarction leads to cardiac specific troponins being found in the serum at a magnitude proportional to the degree of myocyte necrosis.

Troponins are basically molecules that are present in the contractile machinery of striated muscle. There are three subunits namely

- Troponin C
- Troponin T
- Troponin I

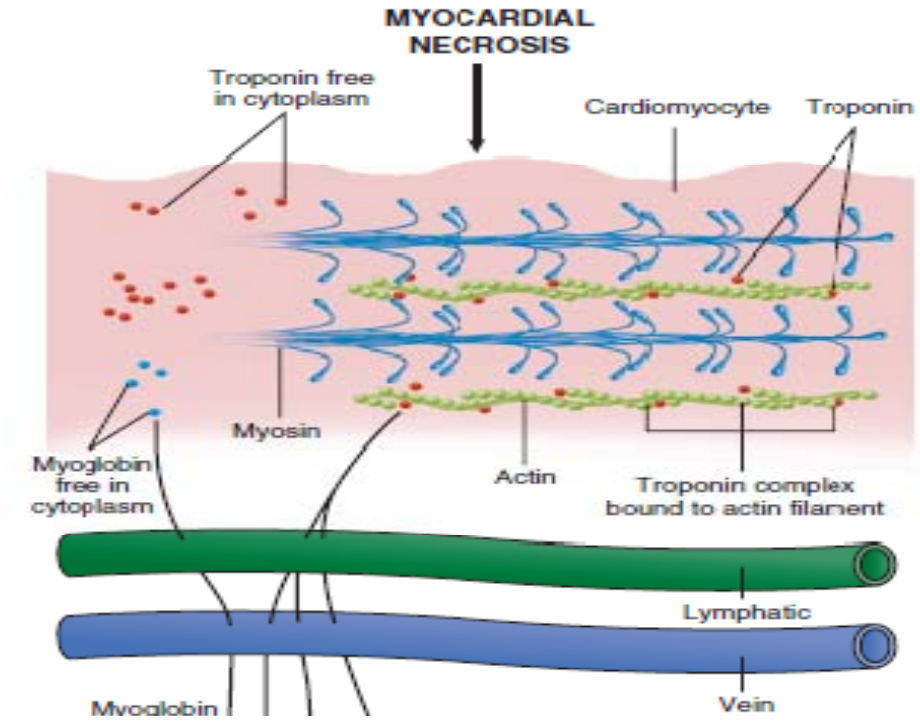
Troponin C binds calcium. Troponin T binds to Tropomyosin and Troponin I binds to actin and inhibits actin – myosin interaction.

Cardiac and skeletal muscle Troponin T and I are encoded by different genes and hence cardiac Troponins are different isoforms from that of skeletal muscle Troponins. Hence specific antibodies specific for cardiac troponins are produced and are made use of in the detection of serum level of these biomarkers.

Most of the Cardiac Troponin T is incorporated into the contractile complex and about 6-8% of it is dissolved in the cytosol, whereas only 2-3% of the Troponin I is dissolved in the cytosol. Following myocyte injury, initially, the cytosolic pool of cardiac Troponins are released into the circulation and subsequently the components in the myofilaments are released into the circulation.[26-27]

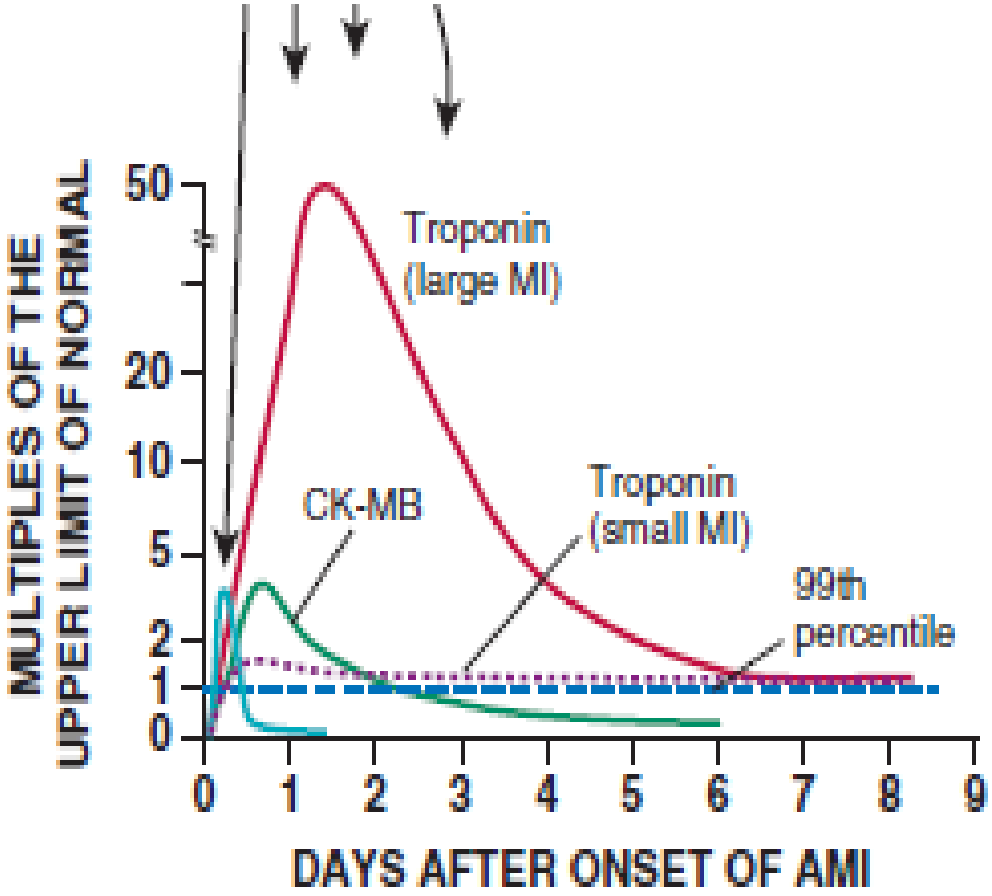
In patients with Myocardial Infarction, cardiac Troponin T and I begin to rise by about 3 hours after the onset of chest pain. Because of continuous release from a degenerating contractile apparatus in necrotic myocytes, elevations in cardiac Troponin I may persist for 7 to 10 days after MI and elevations in cardiac Troponin T may persist for up to 10 to 14 days.

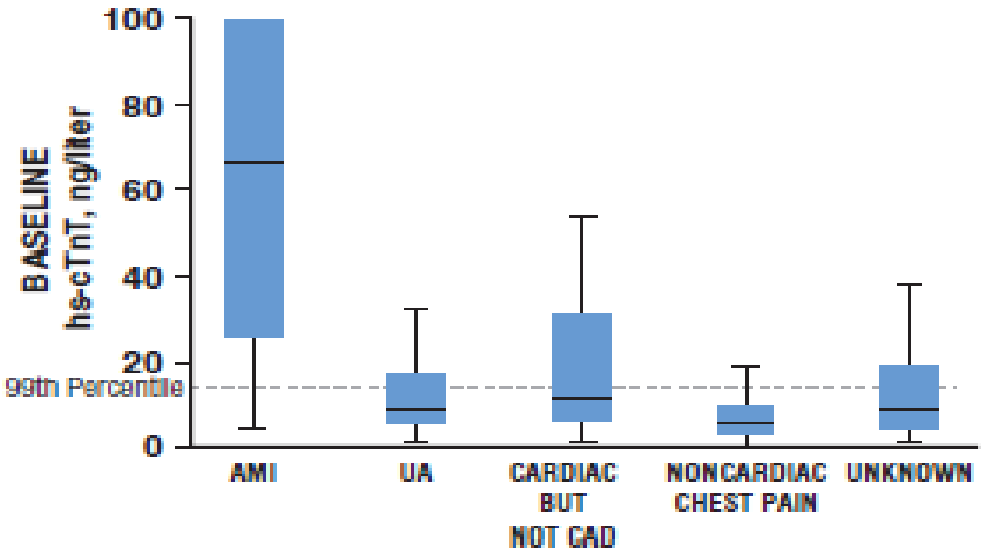
Variations in the cutoff for abnormal levels of cardiac Troponin I in clinically available immunoassays result from the different specificities of the antibodies used for detecting free and complexed cardiac Troponin I. For both the cardiac Troponins, the definition of an abnormally increased level is a value exceeding that of 99% of a reference control group. Assays that have a level of imprecision (coefficient of variation) of less than 10% at the specific 99th percentile cutoff are optimal for clinical practice.



The above image shows the troponin and myoglobin in the myocyte and their release into the circulation following myocyte injury.

The timeline of serum concentrations of various cardiac biomarkers following myocardial infarction:[28]





The graph above depicts the level of rise in serum concentration of highly sensitive cardiac Troponin T above the 99th percentile in various conditions. The same graph holds good for cardiac Troponin T also.

With clear definitions not made for diagnosis, to identify the NSTE-ACS during triage at the Emergency Room, Six et al from Netherlands framed the HEART Score comprising of components from the History of the nature of chest pain, the ECG features of ischemia, Age of the patient, Risk factors, Troponin levels, giving each component an equal weightage in the score, with the score ranging from 0 to 10 was framed.

HEART SCORE

		Points	
History	Highly suspicious	2	
	Moderately suspicious	1	
	Slightly suspicious	0	
EKG	Significant ST-deviation	2	
	Non specific repolarization disturbance / LBTB /PM	1	
	Normal	0	
Age	>65 years	2	
	> 45 an d <65 years	1	
	< 45 years	0	
Risk factors[1]	≥ 3 risk factors	2	
	1 or 2 risk factors	1	
	No risk factors known	0	
Troponin	> 3x normal limit	2	
	> 1 and < 3x normal limit	1	
	≤ 1x normal limit	0	
TOTAL			

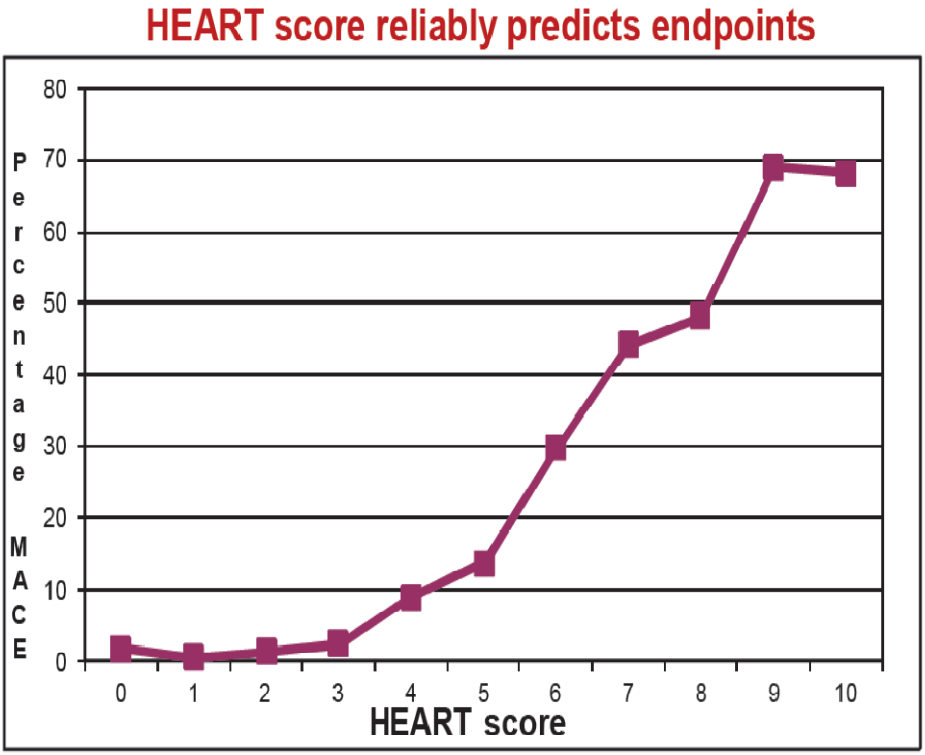
[1] Risk factors: hyperlipidaemia, hypertension, cigarette smoking, diabetes Mellitus, obesity, positive family history

The HEART score was framed at the time of presentation to the emergency room.

The HEART score was framed by Six, Backus et al at Netherlands. Several prospective validation studies have been made to establish the accuracy of the HEART Score by them.

In one prospective validation study by Six et al, published in the International Journal of Cardiology, in 2013,on 2440 patients, looked for the

endpoint of MACE occurring in 6 weeks. The study concluded that the HEART score provides the clinician with a quick and reliable predictor of outcome, without computer-required calculating and that, Low HEART scores (0-3), exclude short-term MACE with >98% certainty and so in those patients that one might consider reserved policies. Also the study concluded that in patients with high HEART scores (7-10) the high risk of MACE may indicate more aggressive policies.[3,4]



Risk groups and proposed policy when using the HEART score (pooled results n=6174)

HEART	~ % pts	MACE/n	MACE	Death	Proposed Policy
0-3	32%	38/1993	1.9%	0.05%	Discharge
4-6	51%	413/3136	13%	1.3%	Observation, risk management
7-10	17%	518/1045	50%	2.8%	Observation, treatment, CAG

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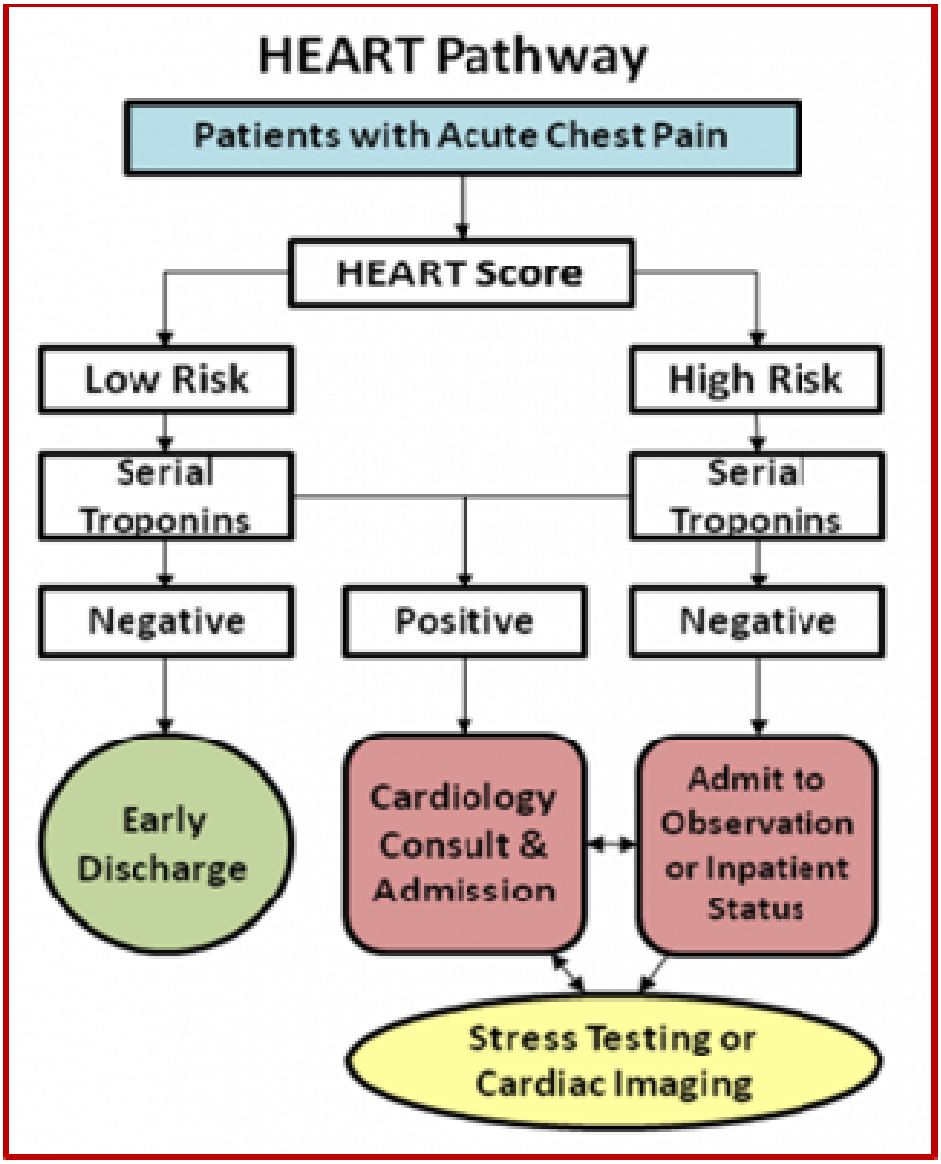
A Prospective validation study of the HEART Score was conducted in Sundaram Medical Foundation, Chennai, India, published in the International Journal of Emergency Medicine in 2015, studied 87 patients with chest pain, with HEART Score following them for the endpoint of occurrence of MACE at 30 days. It found that high HEARTS Score (score of 7 to 10), showed 93% sensitivity and 98% specificity in predicting the occurrence of MACE at 30 days.[5]



In one study, published in the Journal of the American Heart Association, June 2017,[10] the sensitivity of HEART score of 4 or more in identifying NSTE-ACS was found to be around 90% and specificity of around 40%.

	Women	Men
All patients, n	831	1084
NPV	97.9 (95.7–99.2)	93.5 (90.4–95.8)
PPV	15.3 (12.2–18.8)	28.1 (24.8–31.5)
Sensitivity	91.6 (83.4–96.5)	89.3 (84.5–93.0)
Specificity	43.7 (40.1–47.4)	40.0 (36.08–43.4)

Low HEART score, 0 to 3 points; nonlow HEART score, 4 to 10 points (intermediate- and high-risk category). NPV indicates negative predictive value; PPV, positive predictive value.

The shortcomings of the HEART score were that all the components were weighed equally. While Troponin positivity and ECG changes are more definitive in establishing NSTE-ACS, the other components of the score are not objective enough in doing so. Hence by using regression analysis, each component was given a different score.

Also the HEART score, is recorded at the time when the patient presents to the Emergency Room. As the ECG changes of ischemia and Troponin levels are dynamic, the score was modified as HEARTS3 SCORE where the Sex of the patient, Serial ECG at 2nd hour and Serial Troponin levels at 2nd hour are taken into account and the new score of HEARTS3 SCORE was framed. The HEARTS3 Score was developed by Fesmire et al, at University of Tennessee

College of Medicine, Chattanooga, Tennessee, USA, in 2012. They conducted a retrospective analysis in prospectively acquired data in patients with NSTE chest pain, comparing HEART and HEARTS3 Scores. There was a significant difference in area under the ROC for both (0.958 vs 0.825 for HEARTS3 and HEART Scores) for the occurrence of ACS at 30 days. The study concluded that the HEARTS3 Score reliably risk stratified chest pain patients for 30 day ACS, and that PROSPECTIVE Studies needed to be performed to determine implementation of this score can guide decision regarding treatment and disposition in the emergency room.[1.]

HEARTS3 SCORE

HISTORY	HEARTS3 SCORE
PROBABLE NON CARDIAC CHEST PAIN	0
POSSIBLE ISCHEMIC CHEST PAIN	1
PROBABLE ISCHEMIC CHEST PAIN	4
ECG(BASELINE)	
ABSENCE OF ISCHEMIC ECG CHANGES	0
OLD INFARCT/BBB/HYPERTROPHY	1
ISCHAEMIC ST DEPRESSION OR T INVERSION	3
AGE IN YEARS	
<45	0
>45	1

NO.OF RISK FACTORS	
0 TO 2	0
3 TO 6	1
TROPONIN T(BASELINE)	
<THE CUT OFF	0
1-3X THE CUT OFF	2
>3X THE CUT OFF	5
SEX	
FEMALE	0
MALE	1
SERIAL ECG	
NO CHANGE	0
NO DIAGNOSTIC ISCHAEMIC CHANGE	2
DIAGNOSTIC ISCHAEMIC CHANGE	5
SERIAL TROPONIN T AT 2HOURS	
<+0.1ng/ml FROM BASELINE	0
+0.1-0.3ng/ml FROM BASELINE	2
>+0.3ng/ml FROM BASELINE	5

The HEARTS3 Score ranges from 0 to 25.

As time is very crucial, an unstable angina if left untreated may progress on to NSTEMI and STEMI leaving an infarct in the myocardial tissue. The ultimate aim is to salvage the myocardium from infarction.

MATERIAL AND METHODOLOGY

STUDY DESIGN:

Prospective observational study

STUDY PERIOD:

6 months

STUDY AREA:

Government Kilpauk Medical College Hospital.

STUDY POPULATION:

Adults, 18 years and older presenting with chief complaints of chest pain to the Emergency Room in Government Kilpauk Medical College Hospital, Chennai, during the study period January 2018 to June 2018, were included in the study.

SAMPLE SIZE

The sample size is calculated using Openepi application, with Confidence level of 95%, proportion with outcome (MACE) of 30% and accuracy (absolute) of 20%, and the sample size is found to be 100.

INCLUSION CRITERIA

Adults, 18 years and older of either gender, presenting with chief complaints of chest pain to the emergency room.

EXCLUSION CRITERIA

All patients presenting with STEMI are excluded from the study.

METHODOLOGY

We were informed about the arrival of the patients meeting the inclusion criteria, presenting at the Emergency Room of Kilpauk Medical College Hospital by the attending duty physician at the emergency room at any time 24x7.With the informed written consent from the patient, the patient will be enrolled in the study. The HEARTS3 score was framed for the patient with the History, ECG, Age, history of Risk factors, Troponin, Sex, Serial ECG and Serial troponin at 2 hours.

The patient was followed up and was observed for any Major Adverse Cardiac Event (MACE), such as Myocardial Infarction, Cardiogenic shock, Cardiac arrest, all cause cardiac death, upto 7 days of initial presentation.

CASE DEFINITION

HISTORY

The patient's typicality of chest pain will be assessed from the history. As guided by the 2014 AHA ACC guideline for NSTEMI ACS, NSTEMI ACS[11] most commonly presents as a pressure-type chest pain that typically occurs at rest or minimal exertion lasting for 10 minutes or more. The patients presenting with all the characteristics mentioned above are classified to have probable ischemic chest pain.

The patients presenting with some of the above mentioned characteristics of chest pain are classified to have possible ischemic chest pain.

Features not characteristic of ischemic chest pain include[18]:

- Pleuritic pain(sharp or knifelike pain provoked by respiration or cough);
- Primary or sole location of discomfort in the middle or lower abdomen;
- Pain localized by the tip of 1 finger, particularly at the left ventricular apex or costochondral junction;
- Pain reproduced with movement or palpation of the chest wall or arms;
- Brief episodes of pain lasting a few seconds or less;
- Pain that is of maximal intensity at onset; and
- Pain that radiates to lower extremities.

The patients presenting with any one of the above mentioned presentations are classified to have probable Non cardiac chest pain.

ECG

An ECG is obtained on arrival to the emergency room and is looked for the presence of ST segment elevation in continuous leads and they are excluded from the study. ECG with straightline or downsloaping ST depression 0.05mV or more or symmetrical T inversion 0.2mV or more in continuous leads are grouped as probable ischemia and are given 3 points.

The presence of chamber hypertrophy, old infarct or bundle branch block on ECG can confound changes of ACS and are grouped to have possible ischemia and are given 1 point.

The ECG is repeated after 2 hours of presentation and is looked for the appearance of ischemic change and points are given as per the table given further.

AGE

Points are given as per the patient's age

RISK FACTORS

The number of risk factors present among Diabetes mellitus, hypertension, hyperlipidemia, smoking in the past 1 month, family history of Coronary Artery Disease will be enquired and the patient's BMI will be measured and will be categorized for obesity if the BMI is 30 kg/sq.meter or more. Points will be given as per the number of risk factors present

TROPONIN

The patient's blood is drawn and Troponin T levels are measured on arrival and is taken as the baseline Troponin T. The 99^{th} percentile of the upper reference level as determined by the lab is taken as the cut-off and is given points according to whether the Baseline Troponin T is below the cut off or 1 to 3 times the cut off or more than 3 times the cut off.

SEX

Point given depends on the gender.

STATISTICAL ANALYSIS

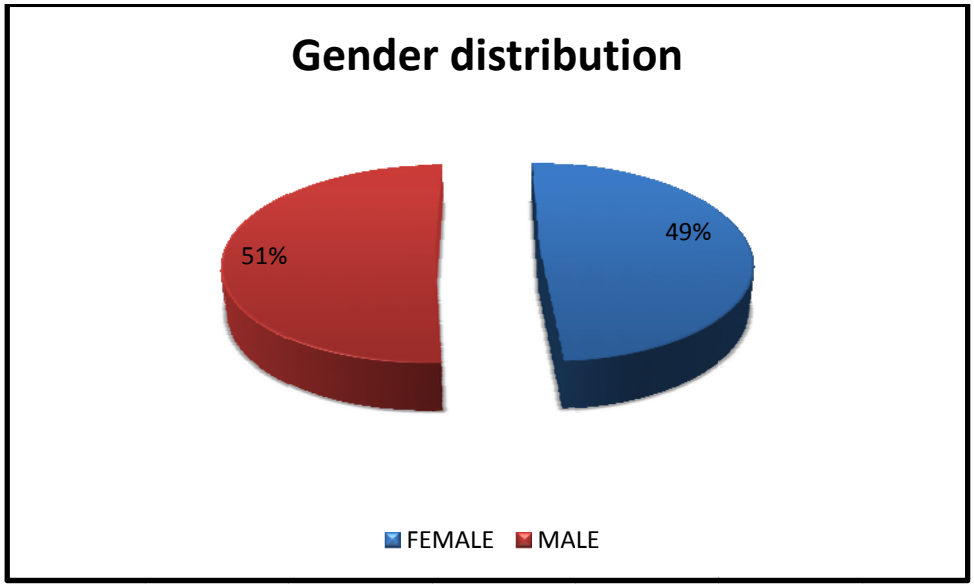
The data was collected in the master chart obtained in the Microsoft excel format.

The collected data were analysed with IBM.SPSS statistics software 23.0 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the efficacy of theHEARTS3 Score, Sensitivity, Specificity, PPV and NPV and diagnostic accuracy with Receiver Operating Curve (ROC) was used. In the above statistical tool the probability value .05 is considered as significant level.

RESULTS

The number of subjects enrolled in my study were 100.

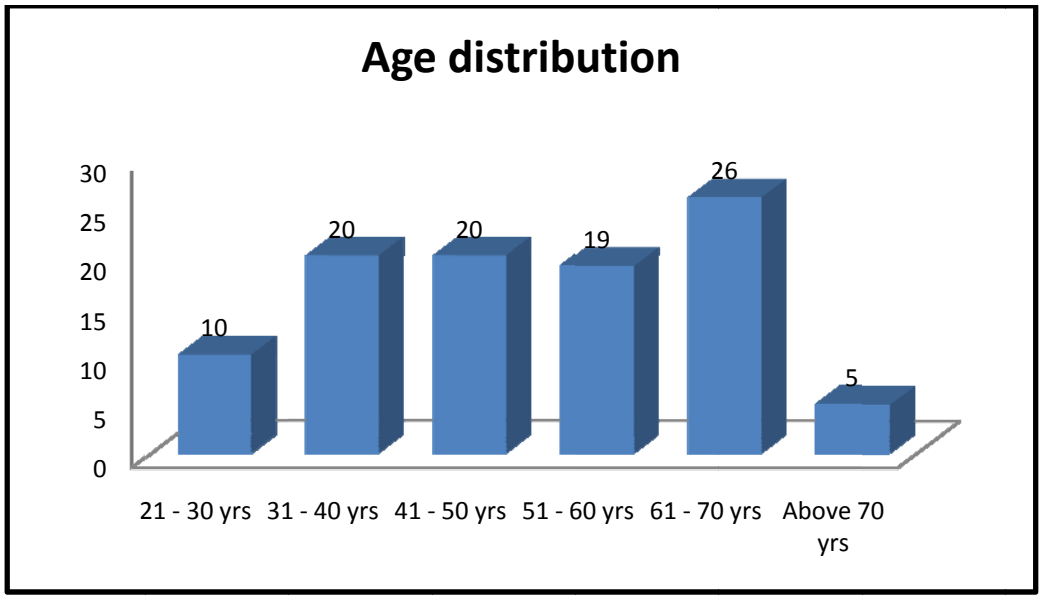
Of the 100 subjects studied, 51 were males and 49 were females, accounting to 51% males and 49% females, which is shown in the frequency table and pie chart below.



GENDER

		Frequency	Percent
Valid	MALE	51	51.0
	FEMALE	49	49.0
	Total	100	100.0

Of the 100 subjects enrolled in the study, number of subjects of age from 21 to 30 years were 10, between 31 to 40 years were 20, 41 to 50 years were 20, 51 to 60 years were 19, 61 to 70 years were 26 and above 70 years were 5, respectively making 10%, 20%, 20%, 19%, 26% and 5% of the study population, and the lowest age of the subject included in the study is 23 years and the highest age is 76 years , the range being 53 and the mean age of the study subjects is 50.80 years, which is shown in the frequency table and bar diagram as below. The Y axis shows the number of subjects.



AGE

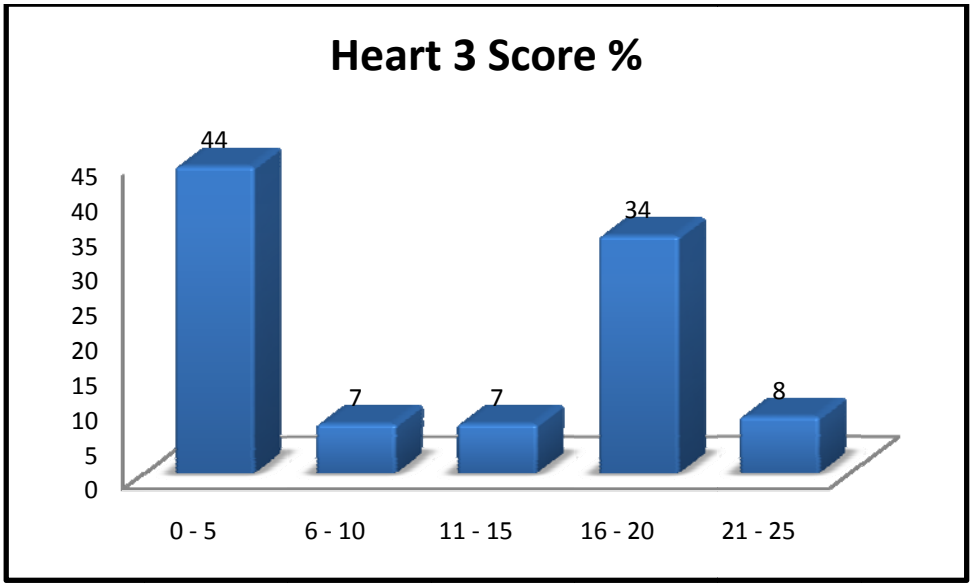
		Frequency	Percent
Valid	21 - 30 yrs	10	10.0
	31 - 40 yrs	20	20.0
	41 - 50 yrs	20	20.0
	51 - 60 yrs	19	19.0
	61 - 70 yrs	26	26.0
	Above 70 yrs	5	5.0
	Total	100	100.0

	N	Minimum	Maximum	Mean	Std. Deviation
AGE	100	23	76	50.80	14.311
Valid N (listwise)					

Of the 100 subjects, 44 had HEARTS3 Score from 0-5, accounting for 44%, 7 had score from 6-10, accounting for 7%, 7 had score from 11-15, accounting for 7%, 34 had score from 16-20, accounting for 34% and 8 had score from 21-25, accounting for 8%.

HEARTS3 SCORE

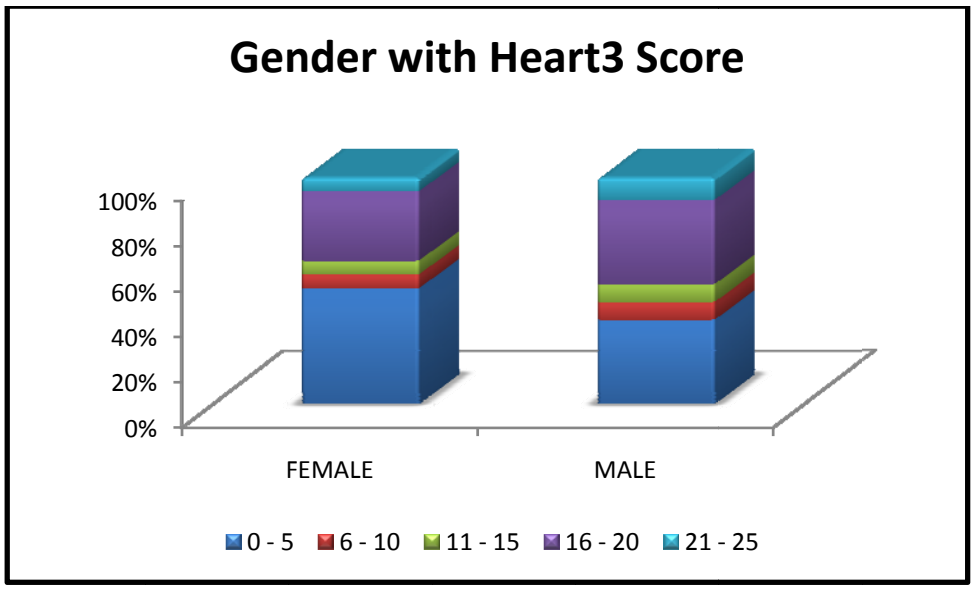
	Frequency	Percent
0 - 5	44	44.0
6 - 10	7	7.0
11-15	7	7.0
16-20	34	34.0
21-25	8	8.0
Total	100	100.0



The gender distribution of various HEARTS3 Score subgroups are shown below:

HEARTS3 SCORE GENDER Cross tabulation

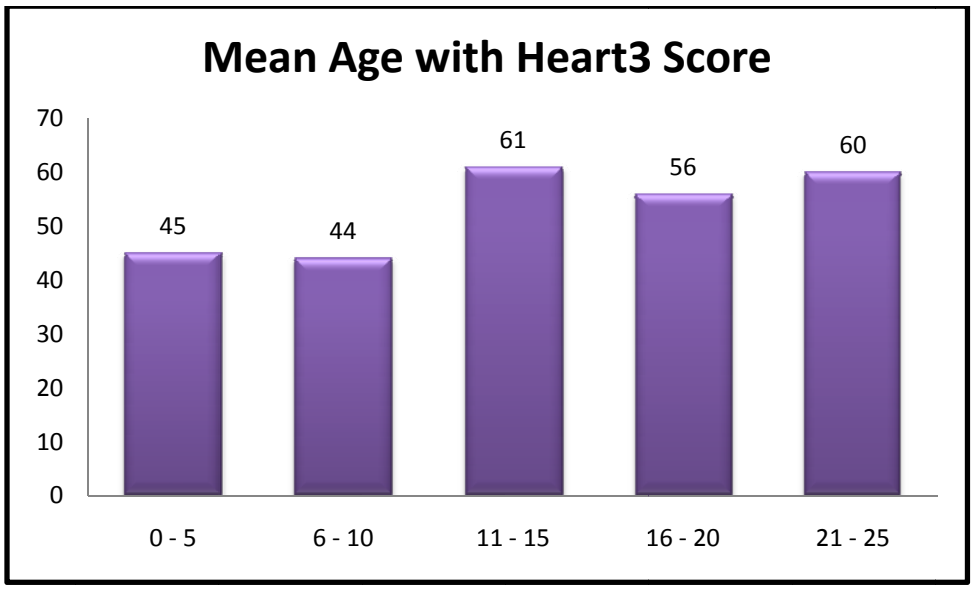
HEARTS3 SCORE		GENDER		Total
		MALE	FEMALE	
0- 5	Count	19	25	44
	% within GENDER	37.3%	51%	44.0%
6-10	Count	4	3	7
	% within GENDER	7.8%	6.1%	7.0%
11 - 15	Count	4	3	7
	% within GENDER	7.8%	6.1%	7.0%
16 - 20	Count	19	15	34
	% within GENDER	37.3%	30.6%	34.0%
21 - 25	Count	5	3	8
	% within GENDER	9.8%	6.1%	8.0%
Total	Count	51	49	100
	% within GENDER	100.0%	100.0%	100.0%



From, the gender distribution it is found that of the subjects with HEARTS3 Score 16-20, 55.8% (19/34) were males and 44.1% (15/34) were females. Whereas, of the subjects with HEARTS3 Score 21-25, 62.5% (5/8) were males and 37.5% (3/8) were females.

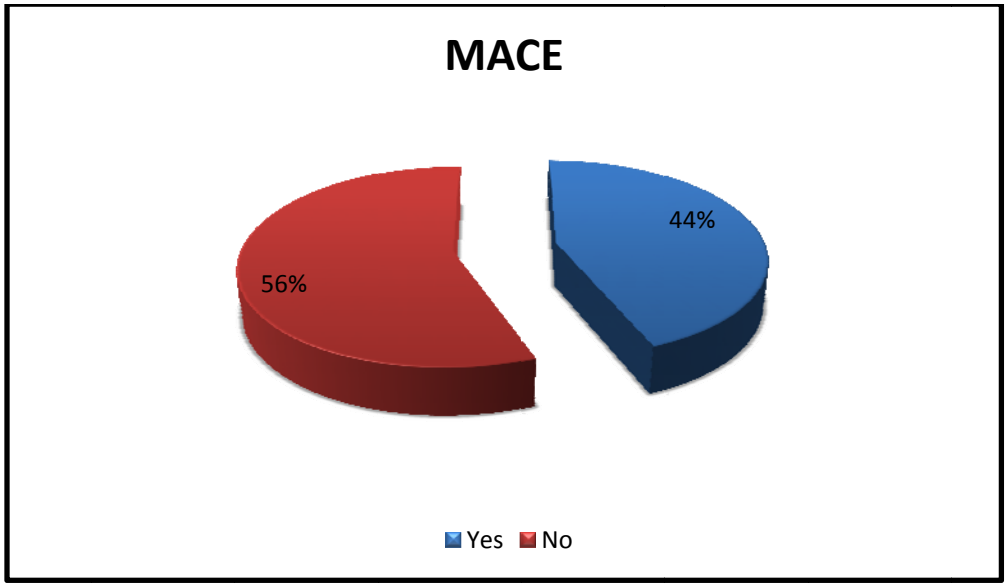
The age distribution for various HEARTS3 Score subgroups are studied and the mean age of the subjects in each score subgroup is shown in the graph:

The Y axis shows the age in years.



Score	NO.	Mean Age	Standard Deviation	Std. Error	95% Confidence Interval for Mean		Minimum age	Maximum age
					Lower Bound	Upper Bound		
0 - 5	44	45	14.880	2.243	40.18	49.23	23	76
6 - 10	7	44	15.207	5.748	30.22	58.35	26	70
11 - 15	7	61	7.128	2.694	54.55	67.74	49	68
16 - 20	34	56	10.627	1.822	52.03	59.44	36	73
21 - 25	8	60	12.817	4.532	49.28	70.72	40	76
Total	100	51	14.311	1.431	47.96	53.64	23	76

Of the 100 subjects, 44 of them had the outcome, Major Adverse Cardiac Event in the form of myocardial infarction as evidenced by Regional Wall motion abnormality on the Echocardiogram, accounting for 44% and 56 of the subjects did not have any Major Adverse Cardiac Event, accounting for 56% and is depicted as follows:



MACE

		Frequency	Percent
Valid	Yes	44	44.0
	No	56	56.0
	Total	100	100.0

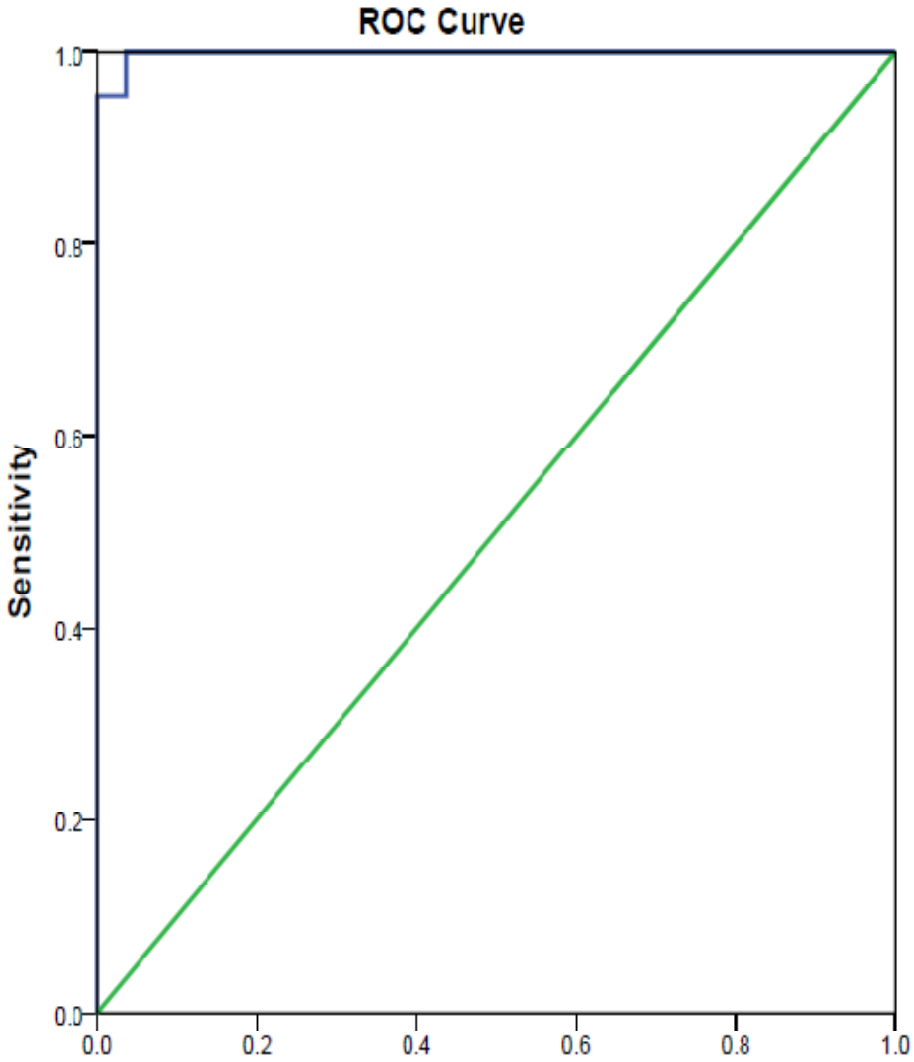
Sensitivity and specificity were found out for each HEARTS3 Score as cut off and are tabulated below:

Coordinates of the Curve

Test Result Variable(s): HEARTS3 SCORE

Positive if Greater Than or Equal To[a]	Sensitivity	1-Specificity
-1.00	1.000	1.000
.50	1.000	.982
1.50	1.000	.875
2.50	1.000	.750
3.50	1.000	.589
4.50	1.000	.375
6.00	1.000	.214
7.50	1.000	.179
8.50	1.000	.143
9.50	1.000	.125
11.00	1.000	.089
13.00	1.000	.036
14.50	.955	.036
16.00	.955	0.000
17.50	.750	0.000
18.50	.432	0.000
19.50	.318	0.000
20.50	.182	0.000
21.50	.091	0.000
22.50	.045	0.000
23.50	.023	0.000
25.00	0.000	0.000

The ROC Curve is plotted with the above tabulated true positive and false positive values as coordinates for each HEARTS3 Score as cut off and the ROC Curve was obtained as follows:



The Area Under the ROC Curve is 0.998 and standard error is 0.002, determined with confidence interval of 99.5% (p value =0.005), which is shown below.

Area Under the Curve

Test Result Variable(s): HEARTS3 SCORE

Area	Std. Error[a]	Asymptotic Sig.[b]	Confidence Interval	
			Lower Bound	Upper Bound
.998	.002	.0005	.995	1.000

a. Under the nonparametric assumption

b. Null hypothesis: true area =0.5

P - Value	** Highly Significant at P ≤ .01

Based on the collected data of this study, on taking HEARTS3 Score cut off of 16 and below as low score and HEARTS3 score more than 16 as high score, Specificity was found to be 100% and sensitivity of 95.45%. Of the 100 subjects studied, 58 of them had low score and 42 had high score.

All the 42 subjects with high score had MACE (outcome) on observing upto 7 days. Of the 58 subjects with low score, 2 had MACE and 56 did not have MACE on observing upto 7 days, which is shown in the confusion matrix as follows:

HEARTS3 SCORE * MACE Cross tabulation

Count

		MACE		Total
		Yes	No	
HEARTS3 SCORE	> 16	42	0	42
	<= 16	2	56	58
Total		44	56	100

Cut off	16
Sensitivity	95.45
Specificity	100.00
PPV	100.00
NPV	96.55
Accuracy	97.73

For the above cut off limit of HEARTS3 score, Positive Predictive Value for MACE is 100% and Negative Predictive value is 96.55% and the accuracy is 97.73%.

DISCUSSION

Acute Coronary Syndrome, comprising of Unstable Angina, and Non ST segment Elevation Myocardial Infarction known as NSTEMI and ST segment Elevation Myocardial Infarction known as STEMI is the commonest etiology of acute chest pain that is life threatening. As their name goes, these conditions namely Unstable Angina and NSTEMI are unstable in that when not recognised on time and managed appropriately, the rupture of the unstable atherosclerotic plaque which had led on to these unstable acute coronary syndromes may progress with the platelet plug and the ensuing thrombus going on to occlude the entire lumen of the artery leading to transmural infarction that becomes ST segment Elevation Myocardial infarction.

The ischemic or the infarcted piece of myocardium may lead on to injury currents which can lead onto dangerous tachyarrhythmias like Ventricular Tachycardia which may deteriorate to Ventricular Fibrillation, which is fatal when not managed on a war footing emergency basis. The incidence of these malignant arrhythmias are highest during the first 24 hours of the onset of myocardial ischemia.

The ischemic or infarcted myocardium can lead on to myocardial dysfunction manifesting as cardiac failure the severity of which depends on the size of myocardium hypoperfused. The dysfunction can be as severe to cause cardiogenic shock and / or acute pulmonary edema.

So fearing these complications and managing every patient who presents with acute chest pain to the emergency room with sophisticated cardiac monitoring is expensive. While certain patients present with chest pain that looks seemingly of coronary etiology, the absence of ischemic changes on the ECG at the outset at presentation may baffle us. It is a routine customary to record Serial ECGs for such patients. While what may be possibly ischemic chest pain by what the patient says alone and the first ECG alone may not be helpful in deciding whether to observe or admit or discharge the patient, when ECG changes are absent or not contributory to an underlying ischemic process. Taking into account his risk factors for coronary artery disease still it may be difficult to decide on such patients in the grey zone.

In many resource poor setting, for the benefit of doubt, as to not to MISS an ongoing coronary event, patients are admitted and they are given antiplatelet and antithrombotic agents, based on just the presence of chest pain and ECG features not typical of ischemia. A good fraction of such patients who were subjected to coronary angiograms thereafter did not demonstrate significant coronary arterial disease. There have been observational studies done for the same[9].

This adds to the patient care cost and anxiety.

So to consolidate all the characteristics to a cumulative score that can detect a coronary event as the etiology of the chest pain reliably was needed from which HEART Score was developed, and validated[3,4,5].

To improvise the shortcomings of the HEART Score, HEARTS3 score was formed. The HEARTS3 Score required validation based on prospective studies[1] and this study is a prospective study to validate its efficiency.

Based on the Area Under ROC curve of 0.998, it is shown that HEARTS3 score is an efficient test and with having a cut off of 16 and below as low score and more than 16 as high score, the HEARTS3 scoring system efficiently and reliably segregates patients presenting with chest pain at the emergency room as those would probably land up in MACE in 7 days and those would probably not.

Hence HEARTS3 Score more than 16 suggests that the etiology of chest pain is Acute Coronary Syndrome in patients presenting with chest pain at the ER. Hence such patients can be admitted and those with lower scores can be observed and planned for early discharge.

LIMITATIONS OF THIS STUDY AND SCOPE FOR FUTURE STUDIES:

This study has observed for MACE occurring upto 7 days from the presentation of chest pain. Though this is the time period wherein there is maximum risk of MACE occurrence following ACS, 30 day MACE incidence should be studied to compare efficiency of HEARTS3 Score with the HEART score as previous studies done with HEART Score have observed for 30 day MACE occurrence.

The score takes 2nd hour serial ECG and 2nd hour Troponin, thus making the score available only by the end of 2nd hour. The score can be modified to HEARTS Score(rather than previous HEART) omitting 2nd hour serial values and ECG to be obtained at the time spot of presentation and validated for a Cutoff value for ACS. And if the cutoff is not met with the HEARTS Score, ie., low HEARTS score, patient may be proceeded to have the full HEARTS3 Score at the end of 2 hours of presentation, before the patient be considered for early discharge.

With point of care Echocardiographic imaging being available and physicians are being made to train in rapid echo screening, presence of Regional Wall Motion Abnormality can be incorporated into the score to improvise the score's sensitivity.

Highly Sensitive Troponin T levels may be incorporated into the score, which can be detected earlier than the Troponin, which may improve the

sensitivity of the HEARTS score at the time when patient presents to the Emergency Room.

CONCLUSION

Chest pain is a common presentation at the Emergency Room. Rapid identification of ACS is a crucial component of the triage.

HEARTS3 Score is an efficient score in triaging acute chest pain patients at the Emergency Room.

Patients with score more than 16 are more likely to have acute coronary syndrome and may be managed in Coronary Care Unit and those with **lower scores may be planned for early discharge,** hence avoiding the generalised use of cardiac monitoring for all patients with chest pain, hence decreasing cost and patient anxiety.

SUMMARY

There was no objective score to triage chest pain patients in the emergency room prior to 2008. Then there came the HEART Score by Six, Backus et al. The shortcomings of the HEART Score were overcome by the improvised form of the score called the HEARTS3 Score.

The HEARTS3 Score has been shown to be more accurate than the HEART Score in effectively picking up ACS. But the efficacy of the HEARTS3 Scoe has not been validated by prospective studies.

My study is a prospective observational study to validate the accuracy of the HEARTS3 Score. The HEARTS3 Score of more than 16 is 100% specific for ACS and 95.45% sensitive.

Hence HEARTS3 score can be used in the emergency room triage protocol for chest pain with scores more than 16 being managed in coronary care units and scores of 16 and less may be planned for early discharge or observation.

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ANNEXURES:

PROFORMA

Name : Age : Sex:

Address : IP / OP No:

Date: Time of presentation at the ER:

Contact No :

Height

Weight

BMI

Chest pain: Character of pain:

Onset of pain during:

Pain since:

Any other detail of the chest pain

ECG finding at presentation

RISK FACTORS:

- Diabetes mellitus
- Hypertension
- Dyslipidemia
- Family history of CAD
- Smoking in the last 1 month
- Obesity

TROPONIN T level at presentation

Serial ECG finding at 2 hours after arrival

Serial Troponin T level at 2 hours after arrival

HEARTS3 SCORE:

MASTER CHART

S.NO	AGE	GENDER	HISTORY	ECG(BASELINE)	AGE	RISK FACTORS	TROPONIN (BASELINE)	SEX	SERIAL ECG	SERIAL TROPONIN	HEARTS3 SCORE	OCCURRENCE OF MACE UPTO 7 DAYS
1	60	MALE	4	1	1	1	2	1	5	5	20	YES
2	48	MALE	4	3	1	1	2	1	2	5	19	YES
3	68	MALE	1	1	1	1	2	1	5	5	17	YES
4	45	MALE	4	3	1	1	2	1	5	2	19	YES
5	56	MALE	4	1	1	1	2	1	2	5	17	YES
6	64	MALE	4	3	1	1	0	1	5	5	20	YES
7	73	MALE	4	1	1	0	2	1	5	5	19	YES
8	48	MALE	1	3	1	1	5	1	5	2	19	YES
9	59	MALE	4	3	1	1	2	1	5	2	19	YES
10	70	MALE	4	3	1	0	5	1	2	5	21	YES
11	58	MALE	4	3	1	1	5	1	5	2	22	YES
12	62	MALE	1	1	1	1	2	1	5	2	14	YES
13	60	MALE	4	3	1	1	0	1	5	5	20	YES
14	45	MALE	1	5	1	1	2	1	5	2	18	YES
15	66	MALE	4	3	1	1	2	1	5	5	22	YES
16	44	MALE	4	1	0	1	3	1	2	5	17	YES
17	43	MALE	4	3	0	1	5	1	5	5	24	YES
18	40	MALE	0	3	0	1	2	1	5	5	17	YES
19	44	MALE	4	1	0	1	0	1	5	5	17	YES
20	41	MALE	1	1	0	0	5	1	5	5	18	YES
21	42	MALE	4	0	0	1	2	1	5	5	18	YES
22	38	MALE	1	3	0	1	5	1	2	5	18	YES
23	42	MALE	4	0	0	0	2	1	5	5	17	YES
24	36	MALE	1	3	0	1	5	1	2	5	18	YES
25	40	MALE	4	3	0	0	5	1	5	5	23	YES
26	62	FEMALE	1	3	1	1	5	0	5	2	18	YES
27	69	FEMALE	4	3	1	1	2	0	2	5	18	YES
28	65	FEMALE	4	3	1	0	5	0	2	5	20	YES
29	70	FEMALE	1	3	1	1	2	0	5	5	18	YES
30	76	FEMALE	4	3	1	1	2	0	5	5	21	YES
31	58	FEMALE	4	1	1	0	5	0	5	2	18	YES
32	59	FEMALE	1	3	1	1	5	0	5	5	21	YES
33	56	FEMALE	4	3	1	1	5	0	2	2	18	YES
34	60	FEMALE	4	0	1	0	2	0	5	5	17	YES
35	62	FEMALE	1	3	1	1	5	0	5	2	18	YES
36	68	FEMALE	1	3	1	1	5	0	5	5	21	YES
37	66	FEMALE	4	1	1	1	0	0	5	5	17	YES
38	55	FEMALE	4	3	1	0	2	0	2	2	14	YES
39	59	FEMALE	0	3	1	1	5	0	5	5	20	YES
40	62	FEMALE	1	3	1	1	5	0	2	5	18	YES
41	68	FEMALE	1	3	1	1	2	0	5	5	18	YES
42	62	FEMALE	4	3	1	1	2	0	5	2	18	YES
43	64	FEMALE	4	1	1	1	0	0	5	5	17	YES
44	59	FEMALE	0	3	1	1	5	0	5	5	20	YES
45	23	MALE	0	1	0	0	0	1	0	0	2	NO
46	36	MALE	4	0	0	0	0	1	2	0	7	NO
47	29	MALE	0	1	0	1	0	1	2	0	5	NO
48	32	MALE	1	1	0	0	0	1	2	2	7	NO
49	26	MALE	0	0	0	1	0	1	2	0	4	NO

50	40	MALE	0	1	0	0	0	1	2	0	4	NO
51	42	MALE	0	0	0	0	0	1	0	0	1	NO
52	40	MALE	1	1	0	1	0	1	0	0	4	NO
53	32	MALE	0	0	0	0	0	1	0	0	1	NO
54	30	MALE	1	1	0	0	0	1	0	0	3	NO
55	45	MALE	1	1	1	0	0	1	0	0	4	NO
56	58	MALE	0	0	1	1	0	1	2	0	5	NO
57	49	MALE	4	1	1	1	2	1	2	0	12	NO
58	48	MALE	0	0	1	0	0	1	0	0	2	NO
59	50	MALE	1	0	1	1	0	1	0	0	4	NO
60	50	MALE	0	1	1	0	0	1	0	0	3	NO
61	70	MALE	1	1	1	1	2	1	2	0	9	NO
62	54	MALE	0	0	1	0	0	1	2	0	4	NO
63	68	MALE	4	1	1	1	2	1	2	0	12	NO
64	72	MALE	0	0	1	1	0	1	2	0	5	NO
65	52	MALE	4	1	1	1	0	1	2	0	10	NO
66	76	MALE	1	0	1	0	0	1	0	0	3	NO
67	62	MALE	0	1	1	0	0	1	2	0	5	NO
68	71	MALE	0	1	1	1	0	1	0	0	4	NO
69	64	MALE	1	0	1	0	0	1	2	0	5	NO
70	66	MALE	4	1	1	1	2	1	2	0	12	NO
71	40	FEMALE	1	0	0	0	0	0	2	0	3	NO
72	36	FEMALE	1	0	0	0	0	0	2	0	3	NO
73	31	FEMALE	0	1	0	0	0	0	0	0	1	NO
74	38	FEMALE	0	1	0	1	0	0	0	0	2	NO
75	26	FEMALE	4	1	0	1	0	0	2	0	8	NO
76	30	FEMALE	0	0	0	0	0	0	0	0	0	NO
77	28	FEMALE	4	0	0	0	0	0	0	0	4	NO
78	26	FEMALE	1	1	0	2	0	0	2	0	5	NO
79	24	FEMALE	1	1	0	2	0	0	0	0	3	NO
80	25	FEMALE	4	0	0	0	0	0	0	0	4	NO
81	36	FEMALE	0	1	0	1	0	0	2	0	4	NO
82	40	FEMALE	4	3	0	1	0	0	2	0	10	NO
83	34	FEMALE	1	0	0	0	0	0	2	0	3	NO
84	43	FEMALE	0	1	0	1	0	0	0	0	2	NO
85	35	FEMALE	4	0	0	0	0	0	0	0	4	NO
86	40	FEMALE	1	1	0	1	0	0	2	0	5	NO
87	44	FEMALE	1	1	0	1	0	0	2	0	5	NO
88	42	FEMALE	0	1	0	1	0	0	0	0	2	NO
89	40	FEMALE	1	0	0	0	0	0	0	0	1	NO
90	38	FEMALE	4	0	0	0	0	0	0	0	4	NO
91	48	FEMALE	0	0	1	0	0	0	2	0	3	NO
92	54	FEMALE	1	3	1	1	0	0	2	0	8	NO
93	67	FEMALE	0	0	1	0	0	0	0	0	1	NO
94	60	FEMALE	4	3	1	1	2	0	2	2	15	NO
95	66	FEMALE	1	0	1	0	0	0	0	0	2	NO
96	55	FEMALE	1	0	1	0	0	0	0	0	2	NO
97	53	FEMALE	1	1	1	0	0	0	0	0	3	NO
98	66	FEMALE	0	0	1	0	0	0	0	0	1	NO
99	68	FEMALE	4	3	1	1	2	0	2	2	15	NO
100	70	FEMALE	4	0	1	0	0	0	0	0	5	NO

சுயஒப்புதல் படிவம்

ஆய்வு செய்யப்படும் தலைப்பு: "அவசரப் பிரிவில் நெஞ்சு வலியின் அபாய அளவை HEARTS3 மதிப்பெண்ணின் வழியாகக் கண்டறியும் துல்லியத்தைப் பரிசோதிக் கும் ஓர் ஆய்வு."

இடம்: பொது மருத்துவத்துவ த் துறை
அரசு கீழ்பாக்கம் மருத்துவக் கல்லூரி மருத்துவமனை
சென்னை

பங்குபெறுபவரின் பெயர் :

பங்குபெறுபவரின் வயது : பங்குபெறுபவரின் எண் : மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டன. நான் இவ்வாய்வில் தன்னிச்சையாக பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த சட்டசிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகிக்கொள்ளல்லாம் என்றும் அறிந்து கொண்டேன்.

இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்து மேலும் ஆய்வு மேற்கொள்ளும்போதும் இந்த ஆய்வில்பங்கு பெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். இந்த ஆய்வின் மூலம் கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக்கொள்ள மறுக்க மாட்டேன்.

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன்.

பங்கேற்பவரின் கையொப்பம் ஆய்வாளரின் கையொப்பம்

இடம் :

தேதி :

PATIENT CONSENT FORM

Study detail**:**

“STUDY TO VALIDATE THE ACCURACY OF HEARTS3 SCORE IN RISK STRATIFYING CHEST PAIN IN THE EMERGENCY ROOM”

Study centre : KILPAUK MEDICAL COLLEGE, CHENNAI

Patients Name :

Patients Age :

Identification Number :

Patient may check (✓) these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ☐

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ☐

I understand that sponsor of the clinical study, others working on the sponsor’s behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ☐

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well-being or any unexpected or unusual symptoms. ☐

I hereby consent to participate in this study. ☐

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests. ☐

Signature/thumb impression:

Patients Name and Address: place date

Signature of investigator :

Study investigator’s Name : place date

S.NO	AGE	GENDER	HISTORY	ECG(BASELINE)	AGE	RISK FACTORS	TROPONIN (BASELINE)	SEX	SERIAL ECG	SERIAL TROPONIN	HEARTS3 SCORE	OCCURRENCE OF MACE UPTO 7 DAYS
1	60	MALE	4	1	1	1	2	1	5	5	20	YES
2	48	MALE	4	3	1	1	2	1	2	5	19	YES
3	68	MALE	1	1	1	1	2	1	5	5	17	YES
4	45	MALE	4	3	1	1	2	1	5	2	19	YES
5	56	MALE	4	1	1	1	2	1	2	5	17	YES
6	64	MALE	4	3	1	1	0	1	5	5	20	YES
7	73	MALE	4	1	1	0	2	1	5	5	19	YES
8	48	MALE	1	3	1	1	5	1	5	2	19	YES
9	59	MALE	4	3	1	1	2	1	5	2	19	YES
10	70	MALE	4	3	1	0	5	1	2	5	21	YES
11	58	MALE	4	3	1	1	5	1	5	2	22	YES
12	62	MALE	1	1	1	1	2	1	5	2	14	YES
13	60	MALE	4	3	1	1	0	1	5	5	20	YES
14	45	MALE	1	5	1	1	2	1	5	2	18	YES
15	66	MALE	4	3	1	1	2	1	5	5	22	YES
16	44	MALE	4	1	0	1	3	1	2	5	17	YES
17	43	MALE	4	3	0	1	5	1	5	5	24	YES
18	40	MALE	0	3	0	1	2	1	5	5	17	YES
19	44	MALE	4	1	0	1	0	1	5	5	17	YES
20	41	MALE	1	1	0	0	5	1	5	5	18	YES
21	42	MALE	4	0	0	1	2	1	5	5	18	YES
22	38	MALE	1	3	0	1	5	1	2	5	18	YES
23	42	MALE	4	0	0	0	2	1	5	5	17	YES
24	36	MALE	1	3	0	1	5	1	2	5	18	YES
25	40	MALE	4	3	0	0	5	1	5	5	23	YES
26	62	FEMALE	1	3	1	1	5	0	5	2	18	YES
27	69	FEMALE	4	3	1	1	2	0	2	5	18	YES
28	65	FEMALE	4	3	1	0	5	0	2	5	20	YES
29	70	FEMALE	1	3	1	1	2	0	5	5	18	YES
30	76	FEMALE	4	3	1	1	2	0	5	5	21	YES
31	58	FEMALE	4	1	1	0	5	0	5	2	18	YES
32	59	FEMALE	1	3	1	1	5	0	5	5	21	YES
33	56	FEMALE	4	3	1	1	5	0	2	2	18	YES
34	60	FEMALE	4	0	1	0	2	0	5	5	17	YES
35	62	FEMALE	1	3	1	1	5	0	5	2	18	YES
36	68	FEMALE	1	3	1	1	5	0	5	5	21	YES
37	66	FEMALE	4	1	1	1	0	0	5	5	17	YES
38	55	FEMALE	4	3	1	0	2	0	2	2	14	YES
39	59	FEMALE	0	3	1	1	5	0	5	5	20	YES
40	62	FEMALE	1	3	1	1	5	0	2	5	18	YES
41	68	FEMALE	1	3	1	1	2	0	5	5	18	YES
42	62	FEMALE	4	3	1	1	2	0	5	2	18	YES
43	64	FEMALE	4	1	1	1	0	0	5	5	17	YES
44	59	FEMALE	0	3	1	1	5	0	5	5	20	YES
45	23	MALE	0	1	0	0	0	1	0	0	2	NO
46	36	MALE	4	0	0	0	0	1	2	0	7	NO
47	29	MALE	0	1	0	1	0	1	2	0	5	NO
48	32	MALE	1	1	0	0	0	1	2	2	7	NO
49	26	MALE	0	0	0	1	0	1	2	0	4	NO

50	40	MALE	0	1	0	0	0	1	2	0	4	NO
51	42	MALE	0	0	0	0	0	1	0	0	1	NO
52	40	MALE	1	1	0	1	0	1	0	0	4	NO
53	32	MALE	0	0	0	0	0	1	0	0	1	NO
54	30	MALE	1	1	0	0	0	1	0	0	3	NO
55	45	MALE	1	1	1	0	0	1	0	0	4	NO
56	58	MALE	0	0	1	1	0	1	2	0	5	NO
57	49	MALE	4	1	1	1	2	1	2	0	12	NO
58	48	MALE	0	0	1	0	0	1	0	0	2	NO
59	50	MALE	1	0	1	1	0	1	0	0	4	NO
60	50	MALE	0	1	1	0	0	1	0	0	3	NO
61	70	MALE	1	1	1	1	2	1	2	0	9	NO
62	54	MALE	0	0	1	0	0	1	2	0	4	NO
63	68	MALE	4	1	1	1	2	1	2	0	12	NO
64	72	MALE	0	0	1	1	0	1	2	0	5	NO
65	52	MALE	4	1	1	1	0	1	2	0	10	NO
66	76	MALE	1	0	1	0	0	1	0	0	3	NO
67	62	MALE	0	1	1	0	0	1	2	0	5	NO
68	71	MALE	0	1	1	1	0	1	0	0	4	NO
69	64	MALE	1	0	1	0	0	1	2	0	5	NO
70	66	MALE	4	1	1	1	2	1	2	0	12	NO
71	40	FEMALE	1	0	0	0	0	0	2	0	3	NO
72	36	FEMALE	1	0	0	0	0	0	2	0	3	NO
73	31	FEMALE	0	1	0	0	0	0	0	0	1	NO
74	38	FEMALE	0	1	0	1	0	0	0	0	2	NO
75	26	FEMALE	4	1	0	1	0	0	2	0	8	NO
76	30	FEMALE	0	0	0	0	0	0	0	0	0	NO
77	28	FEMALE	4	0	0	0	0	0	0	0	4	NO
78	26	FEMALE	1	1	0	2	0	0	2	0	5	NO
79	24	FEMALE	1	1	0	2	0	0	0	0	3	NO
80	25	FEMALE	4	0	0	0	0	0	0	0	4	NO
81	36	FEMALE	0	1	0	1	0	0	2	0	4	NO
82	40	FEMALE	4	3	0	1	0	0	2	0	10	NO
83	34	FEMALE	1	0	0	0	0	0	2	0	3	NO
84	43	FEMALE	0	1	0	1	0	0	0	0	2	NO
85	35	FEMALE	4	0	0	0	0	0	0	0	4	NO
86	40	FEMALE	1	1	0	1	0	0	2	0	5	NO
87	44	FEMALE	1	1	0	1	0	0	2	0	5	NO
88	42	FEMALE	0	1	0	1	0	0	0	0	2	NO
89	40	FEMALE	1	0	0	0	0	0	0	0	1	NO
90	38	FEMALE	4	0	0	0	0	0	0	0	4	NO
91	48	FEMALE	0	0	1	0	0	0	2	0	3	NO
92	54	FEMALE	1	3	1	1	0	0	2	0	8	NO
93	67	FEMALE	0	0	1	0	0	0	0	0	1	NO
94	60	FEMALE	4	3	1	1	2	0	2	2	15	NO
95	66	FEMALE	1	0	1	0	0	0	0	0	2	NO
96	55	FEMALE	1	0	1	0	0	0	0	0	2	NO
97	53	FEMALE	1	1	1	0	0	0	0	0	3	NO
98	66	FEMALE	0	0	1	0	0	0	0	0	1	NO
99	68	FEMALE	4	3	1	1	2	0	2	2	15	NO
100	70	FEMALE	4	0	1	0	0	0	0	0	5	NO